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# American Journal of Obstetrics and Gynecology

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## Original Communications

### A NEW METHOD OF TREATMENT FOR VAGINITIS AND CERVICITIS

SAMUEL L. SIEGLER, M.D., F.A.C.S., BROOKLYN, N. Y.

THE treatment of vaginitis and cervicitis, of bacterial and/or protozoal origin, continues to be of major interest to the gynecologist. While a large proportion of such patients respond with more or less alacrity to the innumerable agents available to the physician today, one often sees cases which are persistently recalcitrant to such treatment and with recurrences which are difficult to avoid because of the many and varied sources of reinfection, as from the urethra, cervix, and the resumption of marital relations.

#### Trends and Modern Treatment

In recent years a more rationally correct approach to this problem has been induced by a better understanding of the biologic characteristics of the normal vagina, with particular reference to the relationship of vaginal pH and vaginal flora. These relationships have been observed by many investigators,<sup>1-4</sup> and a discussion of these is beyond the scope of this report. From accumulated data, however, one may recognize three grades of bacterial flora at varying hydrogen-ion concentrations: normal—Grade I—homogenous bacteria of Döderlein's bacilli (pH 4.0 to 5.7); abnormal—Grade II—Döderlein's bacilli plus other organisms (pH 4.0 to 6.1); and Grade III—organisms other than Döderlein's bacilli (pH 4.9 to 6.9).

Further, Karnaky<sup>5</sup> has shown that when discharges resulting from acute vaginitis were cultured on nutrient agar adjusted to various pH readings, bacterial growths were most abundant at a pH of 7.6 to 8.0, diminishing as the pH was reduced, with little growth below 5.5, and none at or below 4.5. Vaginal pH variations during the normal life cycle and pH ranges, in which various pathologic organisms are observed, are illustrated in Fig. 1. These observations and similar ones by other authors<sup>1-16</sup> have been responsible for the recent empha-

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sis on the use of jellies, tablets, and powders with bases buffered to pH readings approximating the normal, thereby encouraging the elimination of pathologic organisms and the growth of normal vaginal flora consistent with the healthy vagina.

That the rationale for such bases is good has been demonstrated by a number of investigators who have obtained satisfactory results with plain buffered acid jellies, notably Allen and Baum,<sup>6</sup> Karnaky,<sup>5</sup> Bland and Rakoff,<sup>7</sup> Chrisman,<sup>8</sup> and Roblee.<sup>9</sup>

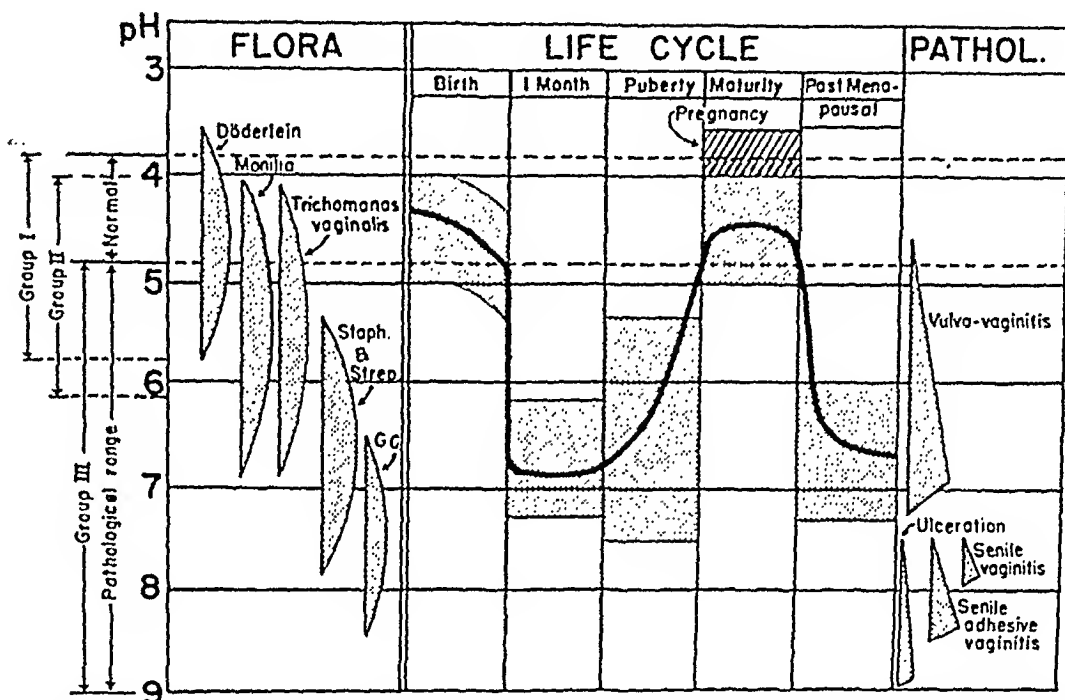


Fig. 1.—Vaginal pH variations during the normal life cycle and pH ranges in which various organisms and vaginal pathology are observed. (Modified from Siegler: Fertility in Women, J. B. Lippincott Co., Philadelphia.)

The emphasis on correctly buffered bases in the treatment of vaginitis and cervicitis has not diminished the desirability of incorporating antiseptic agents into the buffered base. Elden,<sup>10</sup> Karnaky,<sup>11</sup> and Owen<sup>12</sup> employed diodoquin with a buffered lactose powder or tablet base; Brougher<sup>13</sup> used Caprokol in a jelly base; Meigs<sup>14</sup> used acetarsone medicated tampons; Parks<sup>15</sup> and Angelucci<sup>16</sup> used an acid sulfanilamide ointment, and Roblee<sup>9</sup> and Findley<sup>17</sup> used sulfathiazole and sulfanilamide in an acid jelly. They all obtained satisfactory results.

Roblee<sup>9</sup> favored the use of sulfathiazole with his acid jelly, although recognizing that the buffered acid jelly alone was effective in trichomonas vaginitis therapy. Discussing his results, he states, "In our hands the addition of sulfa drugs to the pH factor has been as great an improvement as the pH factor was over older methods of antiseptics used ten years ago in the management of cervicitis and vaginitis." He observed particularly noteworthy results in accelerating the restoration of Type I smear from Type III smear by sulfathiazole and acid jelly, although restoration from Type II smear resulted just as easily from acid jelly alone. He observed excellent results in the control of in-

fections after conization of the infected cervix in cases of acute gonorrhea wherein positive cultures persisted after oral sulfathiazole therapy. Findley<sup>17</sup> likewise obtained gratifying results in the cauterized cervix with sulfanilamide in a buffered acid jelly.

### Desirable Characteristics in the Ideal Anti-Vaginitis-Cervicitis Agents

The author has run the gamut of medicaments for the control of infections in vaginitis and cervicitis from the insufflation of silver pierate, the insertion of medicated suppositories and tampons, capsules of ozonide of olive oil, tablets of beta lactose and sulfonamides, and finally the newer type of acid buffered jellies. A critical evaluation of all these medicaments has led him to conclude that the ideal antiinfective agent should be:

1. As easy as possible to apply by the physician in his office and by the patient at home, because treatment sometimes must be continued by the patient over many days or weeks. Successful results due to patient cooperation can only be expected, if it can be done with the least possible inconvenience.

2. Buffered effectively so as to promote the reestablishment of the physiologically correct acidity and growth of Döderlein's bacilli consistent with a healthy vagina.

3. Antibacterial so as to control rapidly persistent infections especially in cervicitis requiring electrosurgery.

4. Of such a physical consistency as to assure intimate and prolonged contact with vaginal and cervical mucosa. Present-day water-dispersible jellies have been an improvement over powders and tablets. However, the ideal base should dissolve in and should approach in physical characteristics (adhesiveness, consistency, wetting power) the vaginocervical secretions.

5. Nonirritating and nontoxic, even when used over a period of time.

6. Because of the above properties, it should give satisfactory results when used as the single agent of choice in bacterial and protozoal vaginitis and cervicitis of all types.

### A Sulfathiazole Acid Jelly With a New Base

The author believes that the above desirable conditions are most closely approached by an acid jelly, containing sulfathiazole in actual solution, of the following composition:

10.0 per cent sulfathiazole*
3.0 per cent lactic acid
1.0 per cent acetic acid
0.1 per cent sodium tetradecyl sulfate
85.9 per cent polyethylene glycol

The acid jelly base, polyethylene glycol, has all the desired characteristics for vaginal medication. It is nonirritant and nontoxic, has excellent wetting properties, and maintains its jelly consistency at body temperature. It dissolves completely in the vaginal secretions, and possesses the unique property of dissolving large quantities of sulfathiazole which, in turn, become soluble in the

\*Westhiazole Vaginal, Westwood Pharmacal Corp., Buffalo, New York.

secretions. This last property makes this jelly far more sulfa active than it is possible to obtain with the usual suspensions of sulfathiazole.<sup>18</sup> The jelly is sterile and can therefore be used in packs and tampons post surgically. The pH approximates 4.0, the buffering power is large, and there is no excessive leakage from the vagina unless the discharge is copious.

The method of intravaginal administration of jellies, using a collapsible tin tube and lucite applicator, although preferable to older methods, still entails the unnecessary fuss and bother coincident with the transfer of jelly from tube to applicator to vagina and the washing of the applicator by the patient or sterilizing of his applicator by the physician. At the author's suggestion, a single-dose, disposable paper applicator was conceived for use with this sulfathiazole acid jelly. Fig. 2 is a sketch of this paper applicator which is filled with one-fourth ounce of the jelly—sufficient to deliver between five and six cubic centimeters. Its use by patient and physician is convenient and time saving.

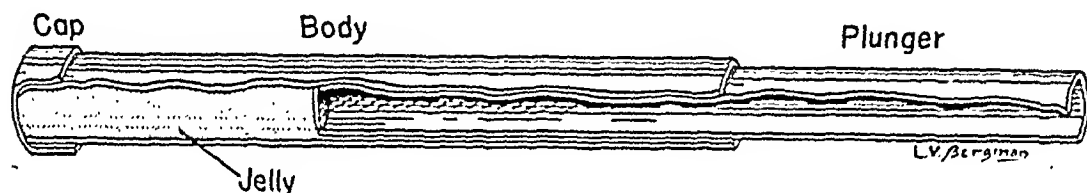


Fig. 2.—Cutaway view of applicator.

### Investigational Data

This report covers a study of the effectiveness of the above-described sulfathiazole acid jelly in the treatment of vaginitis and as an adjunct in the treatment of cervicitis as compared to (1) this same acid jelly base alone, (2) the acid base with 1 per cent iodine, (3) the acid base with 1 per cent gentian violet, (4) beta lactose and sulfathiazole tablets.

The sources of patient material—230 cases of vaginitis and 152 cases of cervicitis, used in this study—were from the author's own private practice and the gynecologic clinics of Unity Hospital and Brooklyn Women's Hospital. In addition to the usual routine records on each patient, the following observations were made on each vaginitis case before, at various times during the treatment, and at the termination of treatment:

1. Urine culture, in catheterized specimens whenever urinary symptoms were present.

2. pH readings with a Beckman meter, using glass electrodes in the vagina and cervix (Figs. 3 and 4).

3. Wet smear and Gram stain—cultures whenever necessary. Similarly complete observations were recorded for each cervicitis case.

Applications of the jellies or tablets were made once or twice daily—one application preferably made at night, before retiring. The use of douches was not permitted. In cervicitis cases treated electrosurgically, these applications were made postoperatively and in a few cases during the waiting necessitated by the proximity of the menses.

The criteria for cure were: complete relief from symptoms, return to normal pH, and negative smears taken at intervals during the three months following termination of treatment. These intervals were: at time of menses, immediately after menses, and at the midperiod.

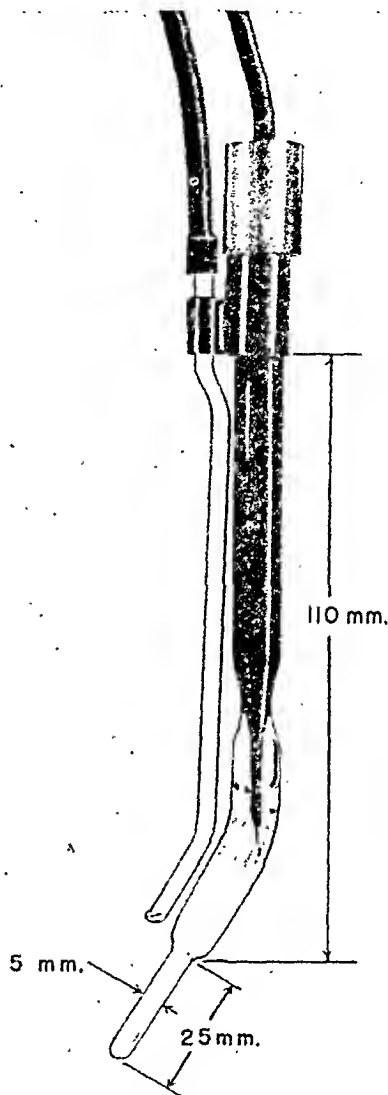


Fig. 3.—Photo-diagram of special cervical and vaginal combination electrode, obtainable from Arthur H. Thomas and Co., Philadelphia, Pa.

Patients in whom symptoms and laboratory findings indicated more or less complete relief, but who had recurrences before these criteria for cure were completely fulfilled, were designated as improved. Patients who discontinued treatment at any time during the course are excluded from this report.

Response of the cervicitis cases to treatment was judged by the character and duration of the discharge, the type of vaginal and cervical smears (or cultures), and the healing time of the lesions to complete epithelialization.

### Results

*Vaginitis Cases.*—Table I summarizes the results following the use of the sulfathiazole-polyethylene glycol acid jelly. About 83 per cent of the cases were considered cured. Ten per cent were considered improved but not cured,

and in 8 per cent, the treatment was ineffective. In the four cases of gonorrheal vaginitis, reported as cured, sulfathiazole was also administered orally. Response to treatment was excellent whether the vaginitis was trichomonal, monilial, or nonspecific in origin.

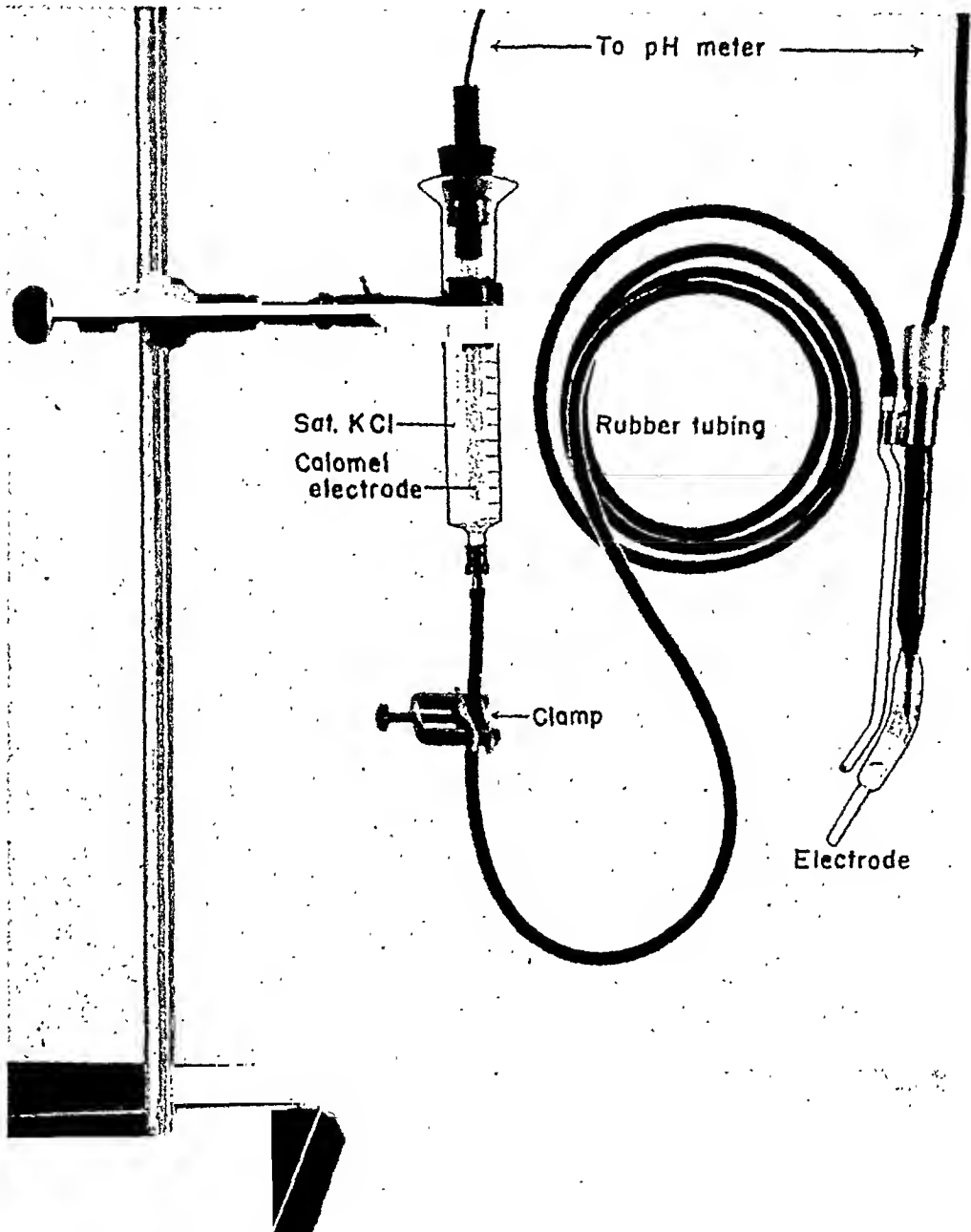


Fig. 4.—Photo-diagram of cervical-vaginal electrode connections. Upper leads go to Beckman pH meter. Pinch clamp permits easy removal of electrode for cleaning. Calomel electrode is suspended in saturated KCl solution in convenient 20 c.c. syringe barrel.

Of the 18 failures, 16 were trichomonas and two monilia. In six of these cases the husband was found to be the cause of continuous reinfection; in two, symptoms were controlled as long as the husband used a condom during coitus.

Duration of treatment before symptoms cleared completely varied from one to seventeen weeks and averaged five and one-half weeks. In most cases

TABLE I. DATA SUMMARY ON 230 VAGINITIS CASES

AGE INCIDENCE		PAROUS STATE		VAGINAL DISCHARGE				VAGINAL SYMPTOMS		VAGINAL EXAMINATION	
CASES	YEARS	PARA	CASES	SYMPTOMS	CASES +	CASES ++	CASES +++	SYMPTOMS	CASES	FINDINGS	CASES
10-20	22	Nulli	94	Amount	30	140	60	Vulvitis	208	Congestion	198
20-30	90	Primi	62	Odor	128	42	6	Irritations		Mucosal petechiae	104
30-40	90	Multi	74	Itch	136	52	14	Vaginal	186	Skene's and Bartholin's	8
40-50	16	Pregnant	22	Bladder symptoms			134	Perirectal	36	Cervicitis	60
50-60	12			Backache			68	Dyspareunia	156	Sacrouterine ligaments tender	46

TYPES OF INFECTION INCIDENCE		NUMERICAL COMPARISON OF RESULTS		DURATION OF TREATMENT BEFORE SYMPTOMS CLEARED	
INFECTION	CASES		CASES	WEEKS	CASES
Trichomonas	142	Cured	190	1- 2	26
Monilia	42	Trichomonas	110	2- 4	48
Monilia and trichomonas	2	Monilia	36	4- 6	42
Mixed (staph. and strep.)	40	Gonococcus	4	6-10	48
Gonococcus	4	Mixed	40	10-15	30
		Improved	22	Over 15	18
		Trichomonas	18		
		Monilia	4		
		Not improved	18		
		Trichomonas	16		
		Monilia	2		

prompt deodorization of the discharge and elimination of itching were obtained. A change in type of smear toward the normal Type I and a lowering in pH to the optimal 4.0 to 5.0 were observed in the improved or cured cases. A mild but definite astringent effect was noted by the patients using the jelly.

Treatment was discontinued in two cases on development of a mild, transient rash and an attack of hives which may have been attributed to sulfathiazole sensitivity. However, repeated determinations of the sulfathiazole level in the blood failed to reveal a demonstrable absorption in any patient.

Twenty-four cases of trichomonas were treated with the polyethylene glycol acid jelly base, with good results in 75 per cent of the cases. The six cases (25 per cent) which failed to respond were subsequently cured on changing to the sulfathiazole jelly.

Twenty-eight cases of monilia responded satisfactorily with the gentian violet polyethylene glycol acid jelly as with the sulfathiazole jelly. However, the two monilia cases in which the sulfathiazole jelly failed also did not respond to subsequent treatment with the gentian violet jelly.

Results were good in six cases of trichomonas treated with 1 per cent iodine in the acid jelly base. However, a chemical burn was produced in two cases, and use of this jelly was therefore discontinued.

Tablets of beta lactose and sulfathiazole were used in ten cases of trichomonas resulting in eight (80 per cent) cures and two (20 per cent) failures



TABLE II. VAGINAL SMEARS AND VAGINAL pH BEFORE AND AFTER TREATMENT—VAGINITIS CASES

TYPE OF SMEAR			VAGINAL pH		
	BEFORE	AFTER		BEFORE	AFTER
TYPE	CASES	CASES	pH	CASES	CASES
<i>Trichomonas Cases:</i>					
I	0	89	4.0-5.0	71	130
II	40	41	5.5-6.0	32	6
III	102	12	6.5-7.5	39	6
<i>Monilia Cases:</i>					
I	0	36	4.0-5.0	26	39
II	16	6	5.5-6.0	16	3
III	28	2	6.5-7.5	2	2
<i>Mixed and Gonococcus Cases:</i>					
I	0	23	4.0-5.0	9	41
II	10	21	5.5-6.0	24	3
III	34	0	6.5-7.5	11	0

TABLE III. DATA SUMMARY ON 152 CERVICITIS CASES

AGE INCIDENCE		PAROUS STATE		MENSTRUAL AND OTHER HISTORY		PREOPERATIVE DISCHARGE	
YEARS	CASES	PARA	CASES	HISTORY	CASES	DISCHARGE	CASES
10-20	2	Nulli	34	Regular	100	Viscid	30
20-30	58	Primi	52	Irregular	32	Mucoid	120
30-40	64	Multi	66	Menopause	20	Purulent	116
40-50	18	Sterile	10	Dysmenorrhea	22	Bleeding	44
50-60	8			Backache	6		
Over 60	2			Uterine fibromyoma	4		
				Postvaginal plastic surgery	6		
				Prolapsed uterus	4		

PREOPERATIVE SMEAR AND/OR CULTURE		PREOPERATIVE CERVICAL LESION		CERVICAL TREATMENT		POSTOPERATIVE BLEEDING INCIDENCE	
BACTERIOLOGY	CASES	CERVICAL LESION	CASES	TREATMENT	CASES	TYPE	CASES
Staphylococcus	4	Cervicitis (acute)	10	Nasal tip	26	Spotting	44
Mixed	102	Chronic cervicitis	82	cantery		Mild hemor-	
Gonococcus	6	Erosions—papillary	36	Conization	46	rhage	
		with cystic changes		Coagulation	44	Primary	4
Negative	40	Lacerations with cystic changes	32	None	34	Secondary	2
Trichomonas	6	Gonococcal cervicitis	6				

which subsequently were cured with the sulfathiazole jelly. This tablet treatment also failed in two nonspecific cases which later cleared with acid polyethylene glycol.

*Cervicitis Cases.*—Table III summarizes the results obtained with the use of the sulfathiazole-polyethylene glycol acid jelly either alone or as an adjunct to electrosurgical cervical treatment.

Nasal-tip cautery was used in 26 cases, conization in 48, coagulation in 44, and no cervical surgery in thirty-four. In all cases the following noteworthy postoperative observations were evident:

1. Absence of foul odor.

2. Absence of profuse discharge; during the sloughing period only slight amounts of thin, watery discharge were observed. This usually disappeared following separation of the slough.

3. Good control of bleeding—only spotting occurred in 44 cases, and slight hemorrhage in six. These occurred at the time of separation of the slough, usually at about the twelfth to fourteenth day. No subsequent surgery was necessary for their control.

4. A mild stenosis was noted in six cases, but pyometra and infection were absent.

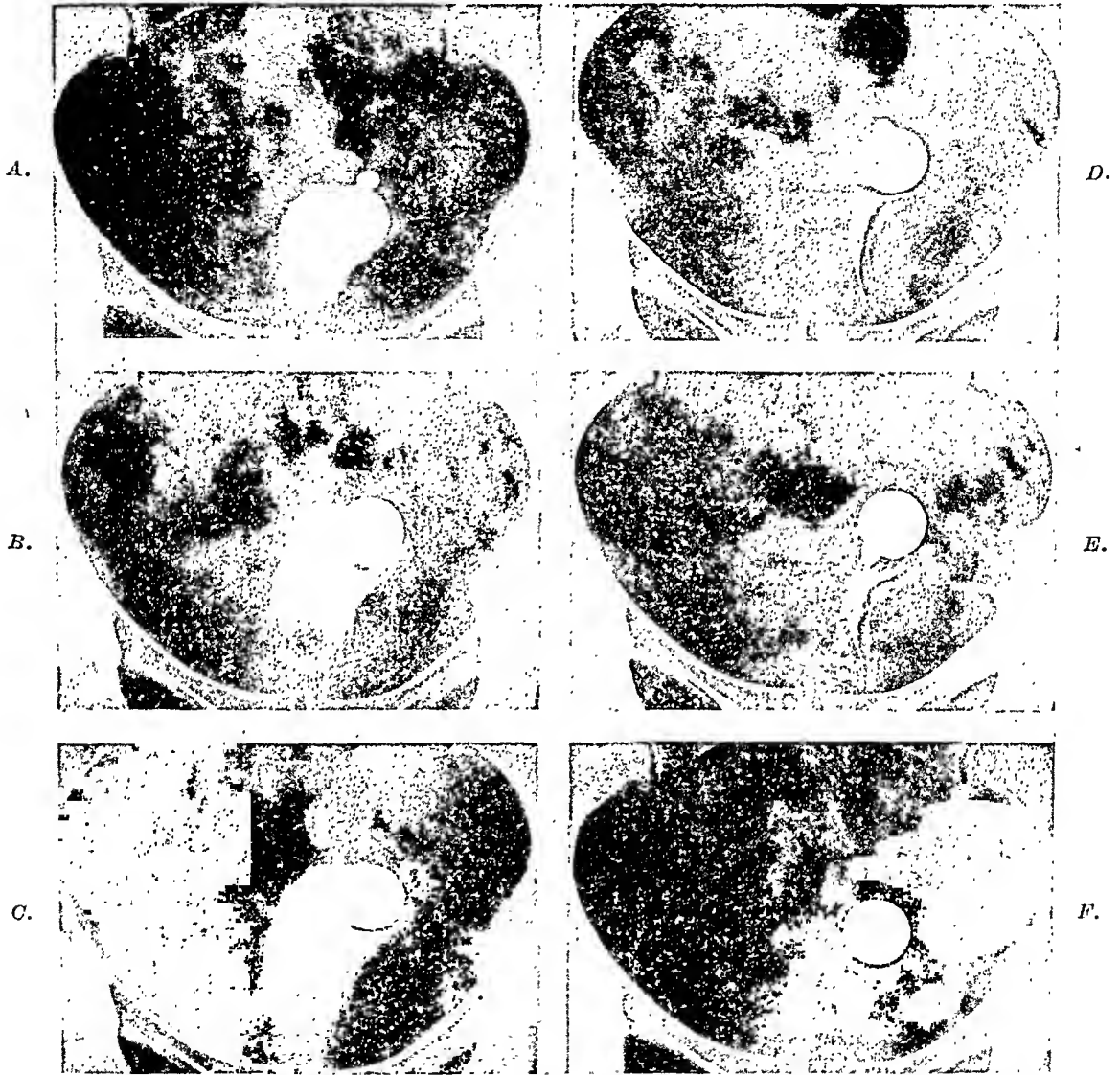


Fig. 5.—Pessary in cervical os and after instillation of 5 c.c. of sulfathiazole jelly plus barium sulfate. (a) Immediately after instillation; after walking and normal activity; (b) one-half hour later; (c) one and one-half hours later; (d) four hours later; (e) eight hours later; (f) twenty-four hours later.

5. In all cases the vaginal pH was between 4.0 and 5.0 at the end of treatment. At this time also the vaginal smear was Type I in 82 per cent of the cases and Type II in the remaining 18 per cent. About 50 per cent of the cases had a cervical pH of between 6.0 and 7.5 before treatment. After treatment this was between pH 8.0 and 8.5 in 92 per cent.

6. A marked reduction in healing time. In 80 per cent of the cases slough removal occurred within two weeks and healing to full epithelization was complete within five weeks in 90 per cent of the cases. This compared favorably

PLATE I

Row A.

Left—Sulfathiazole acid jelly on the cervix, two hours after application.

Center—Cervicitis. Note jelly on cervix twelve hours after application.

Right—Same patient, six weeks later. Daily applications of sulfathiazole acid jelly. No other therapy. Cured.

Row B.

Left—Six hours after application of sulfathiazole acid jelly to cervix; Trichomonas infection.

Center—Cervicitis, two weeks postconization. Note jelly on cervix.

Right—Same patient, healed after five weeks. Daily applications of sulfathiazole acid jelly.

Row C.

Left—Monilia infection, gravid cervix.

Center—Cervicitis, two weeks postnasal tip cantery.

Right—Same patient, healed after four weeks. Daily applications of sulfathiazole acid jelly.

Row D.

Left—Ulcerative cervicitis.

Center—One week postcoagulation.

Right—Same patient, five weeks later. Note sulfathiazole jelly on cervix and with complete epithelization.

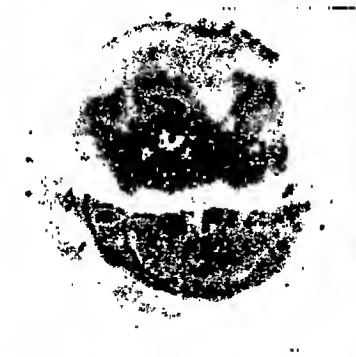
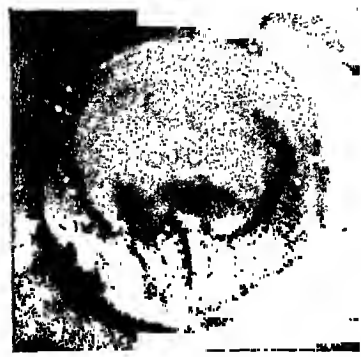
Row E.

Left—Severe vaginitis of Trichomonas origin.

Center—Vaginitis, Monilia.

Right—Vaginitis, with application of  $\frac{1}{4}$  per cent gentian violet acid jelly.

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with Findley's<sup>17</sup> average of seven and one-half weeks without medication and is similar to the results reported by Roblee<sup>9</sup> when using sulfathiazole acid jelly.

TABLE IV. DATA SUMMARY ON CERVICITIS CASES

HEALING TIME			VAGINAL SMEAR TYPE			VAGINAL pH			CERVICAL pH		
WEEKS	SLOUGH CASES	EPITHELIZATION CASES	TYPE	BEFORE CASES	AFTER CASES	pH	BEFORE CASES	AFTER CASES	pH	BEFORE CASES	AFTER CASES
1	22		I	22	124	4.0-5.0	92	152	6.0-6.5	24	4
2	82		II	84	28	5.5-6.0	54		7.0-7.5	50	8
3	4		III	46	0	6.5-7.0	6		8.0-8.5	78	140
4	6	84									
5		52									
6		6									
7	2	6									
+7		4									

The 34 cases wherein the sulfathiazole jelly alone was used also responded gratifyingly well. Healing of the cervical lesions and disappearance of symptoms made superfluous further cervical treatment.

The acid polyethylene jelly base was used in 32 cases with results similar to those obtained with the sulfathiazole jelly, but the infections were not as easily controlled, and healing time was definitely longer. In ten of these cases it was necessary to change to the sulfathiazole jelly to accelerate healing.

### Other Uses

The sulfathiazole-polyethylene glycol acid jelly was also found to control vaginal infections when used after plastic repairs, vaginal hysterectomies, and other vaginal surgery. Here the jelly was impregnated into the usual postoperative pack. When this was removed, one or two daily applications of the jelly were continued until complete healing occurred. Excellent control of postoperative discharge, odor, bleeding, and other symptoms was obtained, as with the cervicitis cases.

Use of the jelly in the cupped end of the Gellhorn pessary, before its insertion for control of prolapsed uterus, was also found to alleviate the odor and discharge usually accompanying such use of the pessary.

### Discussion

An acid polyethylene glycol base, such as used in this study, seems to be the ideal base for intravaginal medication available today. While this base alone is an effective antivaginitis medication, the dissolution of 10 per cent sulfathiazole in it seems to enhance its value in these conditions, probably because of its superior action against secondary bacterial infections. This jelly, because of its adhesiveness, its semiliquid consistency (at body temperature), and its wetting power, assures maximum contact of the medication with vaginal and cervical mucosa. This is indicated by the x-ray reproductions presented in the figures and in the color photographs, Plate I. The appearance of the cervix in some infectious conditions is also illustrated in Plate I.

The sulfathiazole-glycol acid jelly can be used with safety over prolonged periods of treatment, although the possibility of sulfa sensitivity should not be overlooked. In contrast, the insufflation of powders, especially during pregnancies, is a dangerous procedure and can cause fatal accidents, as have been reported recently by Breyfogle,<sup>10</sup> Pierce,<sup>20</sup> Brown,<sup>21</sup> and Partridge.<sup>22</sup>

The well-known observation that the rate of healing of wounds is markedly prolonged by infections has been experimentally confirmed by Howes,<sup>23</sup> who has shown that epithelization is inhibited completely in the presence of infection. In a large proportion of cervical cases treated electrosurgically, pathologic organisms are present in abundance. It is not surprising, therefore, that these surgical lesions heal slowly and with annoying symptoms.

Patient cooperation in maintaining daily, and sometimes necessarily prolonged treatment is more easily obtained with the single-dose, disposable paper applicator than with the usual tin tube and incite applicator.

### Summary

1. A new antivaginitis sulfathiazole polyethylene glycol acid jelly is described.

2. The jelly is nonirritating, nonstaining, and of agreeable odor. It spreads over the cervical and vaginal surfaces and is completely soluble in the secretions. It does not easily leak out of the vagina unless the discharge is profuse. It has a mild but definite astringent effect on the vaginal mucosa.

3. Use of the jelly has resulted in excellent control of vaginitis of trichomonal, monilial, gonococcal, and nonspecific origin in 93 per cent of the cases studied, and in permanent cure in 83 per cent.

4. Use of the jelly alone has given good results in the management of cervical infections in 22 per cent of the cases treated.

5. The period of convalescence can be markedly shortened, and annoying symptoms reduced by using the jelly before and after such procedures as conization, coagulation, cautery, plastic repairs, and other intravaginal surgery. Healing was complete within an average time of five weeks with a minimum of sequelae.

6. The convenience and simplicity of the single-dose disposable paper applicator facilitates intravaginal medication in the office and in the patient's home. This appears to fulfill the therapeutic objective as set forth by the Council on Pharmacy and Chemistry of the American Medical Association<sup>24</sup> in its discussion of antitrichomonas agents, "thoroughness and persistence with the simplest and least messy procedures. . . ."

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# A TEST FOR DETERMINING THE TIME OF OVULATION AND CONCEPTION IN WOMEN\*

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MANY methods have been tried for determining the time of ovulation in women. Hartman<sup>1</sup> and Dickinson<sup>2</sup> have reviewed the literature. Allen, Pratt, Newall, and Bland<sup>3</sup> recovered human ova by washing the oviducts on the fourteenth, fifteenth, and sixteenth days. They concluded that, if the ovum requires seventy-two to ninety-six hours for its transport through the oviduct, ovulation takes place presumably between the twelfth and fourteenth days.

Rock and Hertig<sup>4</sup> removed uteri containing very early embryos at known times of the cycle, and estimated that ovulation occurs from days 13.5 to 19.5 of the cycle. Schroeder,<sup>5</sup> Shaw,<sup>6</sup> Frankel,<sup>7</sup> Ogino,<sup>8</sup> and Meyer<sup>9</sup> reported ovulation to have happened on days 13 to 19, as indicated by macroscopic and microscopic study of the ovary. Dickinson,<sup>10</sup> by manual examination of selected women under specially favorable circumstances, detected changes in the ovary at the time of ovulation.

Papanicolaou,<sup>11</sup> and de Allende, Shorr and Hartman<sup>12</sup> have studied the changes in the vaginal smear in relation to ovulation. Wollner<sup>13</sup> described physical changes in the cervix at that time. Long before ovulation the cervical canal was dry. At ovulation it exhibited a thick, glairy, mucous discharge. Siegler,<sup>14</sup> from endometrial biopsy studies, concluded that menstruation occurs at a period of from twelve to sixteen days after ovulation.

Knaus<sup>15</sup> observed that posterior pituitary extract (puitrin) had no effect on the myometrium during the period that the corpus luteum was active. He assumed that ovulation takes place two to three days before the uterus becomes refractory to the drug, and concluded that ovulation occurs exactly fifteen days before the ensuing menstruation. Ogino<sup>8</sup> confirmed this statement by observing signs of recent ovulation at laparotomy.

D'Amour<sup>16</sup> assayed urine daily for both estrogen and gonadotrophin, and described a gonadotropic peak at the time of ovulation.

Alteration in body temperature during the menstrual cycle, in relation to ovulation and pregnancy, has been the subject of investigation for many years. The temperature of a healthy individual is theoretically 98.6° F. There are slight variations from this figure at about ovulation time. It has been found that a woman's temperature is lower during the first part of the menstrual cycle; at about ovulation time there is a slight dip, followed by a two-fifths to four-fifths of a degree increase in temperature. The temperature then remains at this higher level until the ensuing menstruation.

Zuek,<sup>17</sup> Rubinstein,<sup>18</sup> Tompkins,<sup>19</sup> and others tested the temperature changes at ovulation by means of so-called "timed" conceptions. Couples who were planning a pregnancy agreed to use a selected time for coitus on the basis of

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the temperature shift. Greulich, Morris, and Black<sup>20</sup> correlated the temperature shift at midperiod with ovulation. Several days after the temperature rise, ovulation was confirmed by laparotomy.

Burr, Hill, and Allen<sup>21</sup> described an electrometric technique for registering the time of ovulation.

Mittelschmerz, intermenstrual spotting, and other signs are recognized as indications that ovulation is taking place. Wharton,<sup>22</sup> on the basis of these signs, places ovulation between days 9 and 16 after the onset of menstruation, and Siegler,<sup>14</sup> between days 10 and 18 in patients whose cycles vary between 24 and 33 days. Farris<sup>23</sup> measured the walking activity of twelve healthy women for one to six months. All of these individuals experienced an increase in activity at the midperiod.

Dickinson<sup>2</sup> reported conception occurring from isolated coitus at all times of the cycle. Scymour<sup>24</sup> reported successful impregnations on days 2, 4, and 5 in 28-day cycles, and Guttmacher,<sup>25</sup> Cary,<sup>26</sup> and Siegler,<sup>14</sup> in the practice of isolated artificial insemination, recorded conceptions from days 8 through 19 in cycles of 26 to 30 days.

D'Amour,<sup>27</sup> in comparing methods used in determining the time of ovulation, concluded that: (a) subjective experiences are valueless as tests for ovulation; (b) body temperature fluctuations are not sufficiently regular or clear-cut to be reliable; (c) the uniformity of the results of hormonal assays and vaginal smears confirms the validity of each, in that a certain sequence of events appears typical of the normal cycle; (d) because of its sharpness and its apparently close association with ovulation, the gonadotrophin peak occurring in the midinterval is considered as most indicative of the exact time of ovulation.

The various methods now in use for determining the time of ovulation have certain obvious disadvantages. Some of them, such as laparotomy, have only academic interest. Others, such as change in body temperature and subjective feelings, lack value due to the fact that too much is left to the patients, and because many of them fail to conceive when the so-called ovulation time has been determined. Endometrial biopsies and hormonal assays measure ovulation after the event has occurred. None of the above methods are either very accurate or very practical.

The test to be described supplies a new approach to the problem of determining ovulation time. It is a purely objective method.

### Materials and Methods

In brief, the occurrence of ovulation is detected by the reaction of the ovary of the immature white rat to the urine of the patient. If ovulation is not taking place, the patient's urine has no effect upon the ovary of the rat; if it is taking place, the rat's ovaries become hyperemic.

The details of the test are as follows: Urine passed on arising in the morning is employed. The test animal is an immature Wistar rat between 22 and 25 days of age, and weighing between 30 and 50 grams. Two cubic centimeters of the urine are injected subcutaneously into each of two animals. At the end of two hours the rats are killed by illuminating gas. Their abdomens are opened immediately. Each ovary is inspected and its degree of redness is compared with the colors of the Munsell color chart.

The course of the test is determined in two different months for each individual. The first test is made to determine whether it takes place, and, if so,

the day when the reaction begins, and whether it is entirely normal. The test made the following month, if normal, permits an accurate estimate of the optimum time to perform coitus. During the testing periods of both months coitus is interdicted, because it produces a hyperemia in the rat ovary (Farris<sup>28</sup>).

The day for starting the test depends upon the length and the regularity of the patient's cycles. The testing period covers the five or six days preceding the anticipated date of ovulation, the ovulation period, and three days following it.

It has been found that urine can be kept in a household refrigerator without any preservative for as long as five to six weeks, without any apparent loss in the urine's power to produce a color reaction upon testing. Specimens can be shipped from a distance packed around a container of ice or be frozen solid with dry ice, without losing their potency.

A Munsell color chart provides a graduated color scale in red, for measuring the color of the rat's ovary after injection of the rat with the patient's urine. The 5.0 R Munsell chart contains all of the necessary shades of color required for the test. These standard colors represent equally spaced divisions of the three attributes of color known in the Munsell system of color notation as hue, value, and chroma. The hue of a color indicates its relation to red, yellow, green, blue, and purple; the value, its lightness; and chroma, its strength (or departure from neutral). In recording a color by the Munsell notation system, the symbol for hue is written first, and is followed by a symbol written in fraction form, the numerator indicating the value, and the denominator indicating the chroma (H V/C). For example, a sample which is 5 red in hue, 5 in value, and 8 in chroma is written 5.0 R 5/8.

The color scale shown in Table I facilitates the classifying of the degrees of hyperemia observed in the rat ovary.

TABLE I

HYPEREMIA OF THE RAT OVARY		CORRESPONDING COLOR IN 5.0 R MUNSELL COLOR CHART
None	0	5.8/2-5.6/4
Doubtful	D	5.6/6
Present	1+	5.6/8-5.6/10
Present	2+	5.5/8
Present	3+	5.5/10
Present	4+	5.5/12

Degrees of hyperemia which may be present in the ovary of the rat following the injection of the animal with the patient's urine, and its grading according to the standards of the Munsell Color Chart.

It is important to match the colors under standardized lighting conditions. For this purpose a hood is employed which is painted a neutral gray. A Macbeth Daylight light, Model ADP 20, is suspended 18 inches above the animal board. This light was found to be superior to other artificial lights, and to daylight.

Each ovary is graded as to its degree of hyperemia. The ovary is lifted from the abdomen and is placed on a piece of neutral gray paper one-fourth inch square. When comparing the ovary with the color chart, the colors on the chart that are not being used are masked with a piece of neutral gray paper.

Two rats are used for each specimen of urine to be tested, thus supplying four ovaries for evaluation.

The reaction exhibited by one animal is expressed in terms of the degrees of hyperemia observed in both of its ovaries. Since they do not necessarily exhibit the same degrees of hyperemia, this fact complicates somewhat the classification of the reaction of a given animal. The possible degrees of hyperemia which may occur in the ovaries are presented in Table II. The reaction of an

TABLE II. REACTION OF RAT OVARIES TO HUMAN URINE

HYPEREMIA OF OVARIES		
REACTION, RIGHT	REACTION, LEFT	CLASSIFICATION
Negative	Negative	0
Negative	Faint	0
Faint	Faint	D
Negative	Definite 1	+
Definite 1-4	Definite 1-4	+
0 = Negative, or no hyperemia		
D = Doubtful, or faint hyperemia		
+ = Positive or hyperemia in 4 degrees		

Method of evaluating the hyperemia of the rat's ovaries following administration of the patient's urine.

animal is classified as negative (0) if both ovaries exhibit no hyperemia, or if one ovary shows only a faint degree of hyperemia. If both exhibit a faint degree of hyperemia, the reaction is classified as doubtful (D). The reaction is said to be positive (+) if one ovary alone or both ovaries show a definite hyperemia. The positive reactions are listed in four degrees (1+) (2+) (3+) (4+), according to the amount of hyperemia. The reactions are judged by two individuals, and it is seldom that there is any marked disagreement between them.

### Results

Observations were made upon 100 women. Of these, 12 were unmarried and 88 were married. Of the latter, 76 wished to become pregnant. Fifty of the latter had been inseminated artificially for periods varying from a few months to several years, with no conceptions resulting.

#### *Types of Reactions.*—

The reactions are classified as either normal or abnormal. In the case of a normal reaction there is a definite deepening of the color of the rat ovary for three or four consecutive days near the middle of the menstrual period.

#### *Normal Reactions.*—

The majority of patients show a normal color reaction month after month.

Table III records some of the normal reactions which occurred in 41 subjects. It should be noted that the reactions occurred earlier in the shorter cycles than in the longer ones. For example, in subject L. B. C., with a 21-day cycle, hyperemia appeared on the sixth, seventh, and eighth days. In the case of individual A. F. A., with a cycle of 33 days, hyperemia was not present until days 15, 16, 17, and 18.

Thirty-five women supplied normal reactions during their control tests. Nineteen of them (Table III) had reactions which lasted for three days, and 16 had reactions which lasted for four days.

#### *Pregnancy.*—

A number of patients experiencing normal reactions became pregnant. None experiencing abnormal reactions did so. Ten became pregnant when coitus took place on the third or fourth day of consecutive color reaction. No conceptions occurred when intercourse was delayed until the color reaction had disappeared.

TABLE III. NORMAL REACTIONS\*

SUBJECTS	LENGTH OF CYCLE (DAYS)	DAY OF MENSTRUAL CYCLE																					
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
L. B. C.	21					0	+	+	+	0	0	0	0	0	+	0	0	0					
R. S. S.	21					0	+	+	+	0	0	+	0	0	0	0	0	0					
R. C. W.	22						+	+	+	0	0	0	0	0	0	0	0	0					
L. A. F.	22			0	0		+	+	+	0	+	0	0	0	0	0	0	0					
J. E. C.	23					+	+	+	+	0	0	0	0	0	0	0	0	0					
R. C. W.	24						+	+	+	0	+	0	0	0	0	0	0	0					
M. G.	24				+		+	+	+	0	+	0	0	0	0	0	0	0					
W. F. L.	24						+	+	+	0	+	0	0	0	0	0	0	0					
E. G. M.	24																						
A. D.	25							0	+	+	+	0	0	0	0	0	0	0		0			
M. M.	25								+	+	+	0	0	0	0	0	0	0					
M. G. S.	25								+	+	+	0	0	0	0	0	0	0					
W. H. H.	25								+	+	+	0	0	0	0	0	0	0					
J. K.	25								0	0	0	+	+	+	+	+	+	+					
J. K.	25									0	0	+	+	+	+	+	+	+					
L. S. K.	25										0	0	+	+	+	+	+	+					
I. S.	25										0	0	0	0	0	0	0	0					
R. D.	25										0	0	0	0	0	0	0	0					
C. M.	25											0	0	0	0	0	0	0					
L. S. W.	25												0	0	0	0	0	0					
L. W.	25																						
L. K.	26							0	+	+	+	+	+	+	+	+	+	+					
J. K.	26							0	+	+	+	+	+	+	+	+	+	+					
M. P.	26										+	+	+	+	+	+	+	+					
M. T.	26									0	0	+	+	+	+	+	+	+					
J. K.	26							0	0	0	+	+	+	+	+	+	+	+					
N. M.	26							0	0	0	+	+	+	+	+	+	+	+					



Of 50 patients who were being inseminated artificially at frequent intervals without success, only 11 showed any normal reactions. Eight of these 11 women conceived after the insemination date was chosen according to this test.

#### *Abnormal Reactions.—*

There are four types of abnormal reactions, as shown in Table IV:

1. No color
2. One day only of color
3. Two days only of color
4. Split reaction—one or two days of color, separated by no color for one, two, or more days.

This table records the abnormal reactions of 34 subjects. The 12 patients in Group I were probably anovulatory. With one exception, none of the women who exhibited color reactions of only two days' duration has as yet become pregnant. In this case, coitus took place on the second day of color, which was the last day of color of this patient.

Individuals who had been sterile for a long time exhibited a high incidence of abnormal reactions, but occasionally had normal ones. For example, one patient with regular 25-day cycles showed a normal reaction, and ovulation presumably occurred on day 16. The second following cycle was abnormal. The third and fourth cycles showed abnormal 2-day color reactions on days 10 and 11. The fifth cycle was normal with three days of color, and ovulation presumably occurred on day 11.

The length of the menstrual cycle and the first day of color reaction are plotted in Fig. 1, so that ovulation time may be determined in a relatively simple manner. The coordinates of the points are based on: (1) the length of the menstrual cycle ( $X$ ) in forty women who demonstrated the usual three or four days of color reaction during time of ovulation, and (2) the first day of color reaction ( $Y$ ) in these women. The scatter of the points seems to indicate that the length of the cycle and the first day of color reaction are directly associated, i.e., as the length of the cycle increases, the first day of color is later.

To the paired data (length of cycle in days and first day of color) a line, referred to as the "regression line," has been fitted by the method of "Least Squares" to describe this average relationship. The line, fitted in this manner, in effect bisects the points of the scatter and keeps the sum of the squared deviations from the line a minimum. In the equation of the line,  $Y = a + bX$ , the first constant,  $a$ , determines the level of the line, while the second,  $b$ , indicates the units change in  $Y$  for a one unit change in  $X$ .

The regression equation of Graph 1,  $Y = -10.17 + 0.79X$  indicates that for every one day that is added to the length of the cycle there is an increase of 0.79 days in the first day of color reaction.

In using this equation, values are substituted for  $X$ , the length of the cycle, which has been treated as the independent variable, and values for  $Y$ , the day of first color, are obtained. Thus, an individual with a 25-day cycle would most likely show first color reaction at 9.58 days, or between the ninth and tenth days, obtained as follows:  $Y = -10.17 + (0.79)(25)$ .

The range of the line plus or minus one standard error of estimate is also shown on the graph. The standard error of estimate is a measure of the spread about the line, and within a range of the line, plus or minus one standard error of estimate. Approximately two-thirds of the data lie within this area. In the example cited above, it was estimated that the 25-day cycle would show color on the 9.58th day. To cover possible variations, however, there may be added  $\pm$  so many standard errors of estimate to the 9.58. Since a range of the

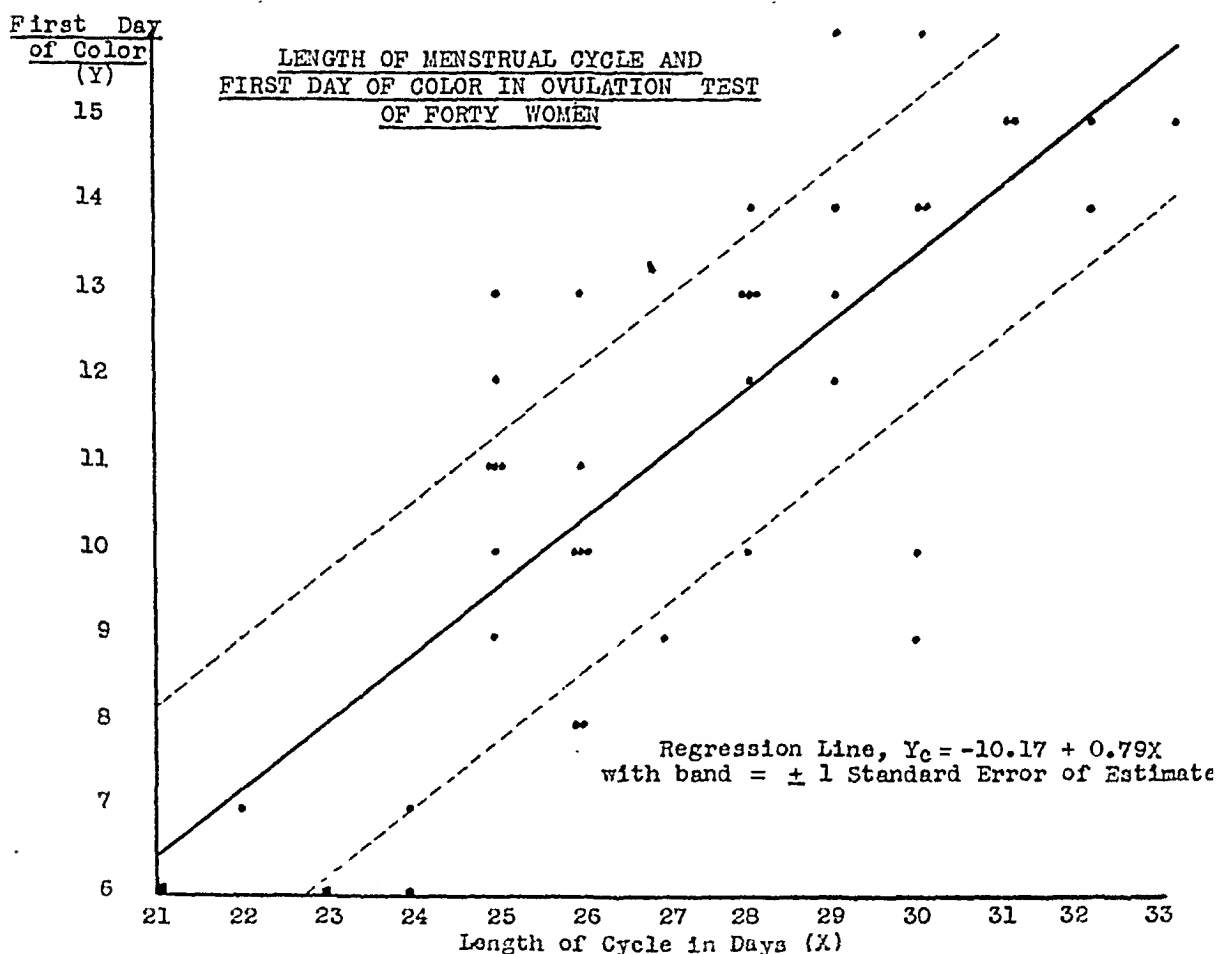


Fig. 1.—The first day of color reaction of forty women, each of whom experienced a normal reaction. The continuous diagonal line represents the days the ovulation process begins, in relation to the length of the cycle. The parallel broken lines represent, between them, the range of possible variation in which two-thirds of the data lie.

To determine time of ovulation in the normal cycle, read the length of the cycle on the horizontal axis. The first day of color is indicated by the value on the diagonal line immediately above this point, and ovulation time by including the first day of color plus two or three additional days for the entire positive color reaction of the test.

estimate plus or minus one standard error of estimate covers approximately two-thirds of the items, the chances are two to one that the observed value will fall within the band indicated by the dotted lines. The standard error of estimate for the 40 pairs studied is 1.8 days. If this be added to and subtracted from 9.58, there is found the range (7.78 to 10.38 days), within which the first day of color reaction will appear in two-thirds of the cases of women with 25-day cycles.\*

\*For the above forty paired items, the coefficient of determination is 0.66 and the coefficient of correlation 0.774. The application of the "t" test to these results indicates that the correlation differs significantly from zero.



TABLE IV. ABNORMAL REACTIONS\*

SUBJECTS	LENGTH OF CYCLE (DAYS)	DAY OF MENSTRUAL CYCLE																						COLOR REACTION
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
<i>Group I</i>																								
E. R. P.	25						0	0	0	0	0	0	0	0	D	0								No color
L. S. K.	25						0	0	0	0	D	0	0	0	0	0								No color
M. G. S.	25						0	0	0	0	0	0	0	0	0	0	0							No color
R. H. L.	26						0	0	0	0	0	D	0	0	0	0	0	0						No color
S. B. B.	28						0	0	0	0	0	0	0	0	D	0								No color
A. A.	28								0	0	0	0	0	0	0	0	0							No color
F. L. M.	28						0	0	0	0	0	0	0	0	0	0	0	D						No color
S. H. R.	29							0	0	0	0	0	0	0	0	0	0	0						No color
J. G. K.	29							0	0	0	0	0	0	0	0	0	0	0						No color
K. M. S.	31								D	0	0	0	0	0	D	0	0	0	D					No color
F. M.	32								0	D	0	0	0	0	D	0	0	0	0					No color
S. R.	35								0	D	0	0	0	0	0	0	0	0	0					No color
<i>Group II</i>																								
M. H.	25						D	0	D	+	0	0	0	0	0	0								One day
L. S.	28										+													One day
<i>Group III</i>																								
K. A.	26						0	0	0	0	+	+	+	0	0	0	0	0	0					Two days
W. H. H.	29										+	+	+	0	0	0	0	0	0					Two days
J. E.	32													0	0	+	0	0	0					Two days
<i>Group IV</i>																								
R. C. W.	22			D	0	0	0	+	0	+	D	0	0	+	0	0	0							Split
M. D. P.	25					0		0	0	+	D	0	0	+	0	0	0							Split
E. K. A.	25	0	0	0	0	+		0	0	+	D	0	0	+	0	0	0							Split
N. G.	25								0	0	D	0	0	+	0	0	0							Split
V. P. C.	25								0	0	D	0	0	+	0	0	0	0						Two days and split
H. E. S.	25								0	0	0	0	+	0	0	0	0							Two days and split
V. P. C.	25						+	0	0	+	D	0	0	+	0	0	0							Two days and split
M. H.	26								0	0	+	0	0	+	0	D	+	0						Split
P. V. P.	26								0	0	+	0	0	+	0	0	0	0	0	+	0			Split
W. F. L.	26								0	0	+	0	0	+	0	0	0	0	0	0	0			Split
E. M.	27								0	0	+	0	0	+	0	0	0	0	0	0	0			Split
I. D.	27								0	0	+	0	0	+	0	0	0	0	0	0	0			Split
S. J. E.	28								0	0	+	0	0	+	0	0	0	0	0	0	0			Split
A. G.	28								0	0	+	0	0	+	0	0	0	0	0	0	0			Split
W. K.	28								0	0	+	0	0	+	0	0	0	0	0	0	0			Split
C. M.	28										+	0	0	+	0	0	D	0	+	0				Split
D. T.	29								0	0	+	0	0	+	0	0	0	0	0	0	0			Split
F. D. M.	31							+	0	+	+	0	0	+	0	0	0	0	0	0	0			Two days and split
N. M.	32								0	+	+	0	0	+	0	0	+	0	0	0	0			Split

36 cycles; 34 different subjects.

+ = Positive color; 0 = no color; D = doubtful reaction.

\*The abnormal reactions which occur in the rat's ovaries following its injection with the patient's urine. Group I shows no color reaction at all during the menstrual cycle. These patients are most likely anovulatory for the particular cycle. Groups II-IV show interrupted or split color reactions.

Patients with abnormal reactions of any kind failed to become pregnant when coitus was planned in relation to the ovulation reaction.

To determine visually the probable first day of color, one should read the length of the cycle on the *X* or horizontal axis. The first day of color will be indicated by the *Y* value of the regression line immediately above this point. The range within which two-thirds of the results should fall may be obtained by reading the *Y* values of the two dotted lines at the given length of the cycle.

Ovulation time is determined by including the first day of color plus two or three additional days for the entire color reaction in the test. For example, a cycle 26 days in length shows first day of color reaction on day 10, to which is added 11, 12, and 13, the three additional days of color reaction. Ovulation should in this case occur on day 13.

*Assays.*—As a check on the clinical aspect of the problem, in an effort to discover what is causing the color reaction, urine specimens were assayed for gonadotrophins.

The amount of gonadotrophin in the urine was assayed by Dr. A. E. Rakoff (method by Levin and Tyndale<sup>20</sup>) on two subjects when the reactions to the present test appeared.

TABLE V. ASSAY DETERMINATIONS OF GONADOTROPHIN\*

DAY OF CYCLE	11	12	13	14	15	16
<i>Subject 1 (First month)</i>						
Two-hour rat test reaction		+	+	2+	+	0
Gonadotropic assay (Mouse units)		24	24	More than 96	None demonstrable	Specimen toxic for animals
<i>Subject 1 (Third month)</i>						
Two-hour rat test reaction	D	+	+	2+	D	0
Gonadotropic assay (Mouse units)	None demonstrable	20	None demonstrable	84	54	Not sent
DAY OF CYCLE	10	11	12	13	14	
<i>Subject 2</i>						
Two-hour rat test reaction	D	+	+	+	+	
Gonadotropic assay (Mouse units)	None Demonstrable	None demonstrable	Toxic specimen	Toxic specimen	42	

D = Doubtful reaction; + = positive reaction or hyperemia; 0 = no color reaction.

\*Assay determinations by gonadotrophin made during the midcycle, when the two-hour rat test revealed color reactions.

Subject 1 (Table V) produced more than 96 mouse units of gonadotrophin on day 14 of the first month, on which day the rat test showed a two-plus reaction. In the following month a two-plus reaction was observed again on the fourteenth day. At this time there were 84 mouse units.

Subject 2 on day 14 produced 42 mouse units of gonadotrophin in the 24-hour sample. The urine samples showed a definite color reaction from days 11 to 14, by the two-hour rat test, and were reported toxic to the test animals in all but one instance by the assay procedure.

D'Amour<sup>16</sup> reported that at the time of ovulation the amount of gonadotrophin produced during a peak varied from 4 to 10 international units. (There is no international unit for pituitary gonadotrophin.) Dr. Rakoff<sup>20</sup>

stated that values between 16 and 32 mouse units of gonadotrophin are considered within the normal range. Occasionally at the peak of gonadotropic activity somewhat higher values may be obtained for a brief period. During the middle of the cycle, when the two-hour rat test showed increased color, the lowest amount of gonadotrophin produced was 20 mouse units, and the highest more than 96 mouse units. It is evident from these findings that the two-hour rat test is extremely sensitive to very small amounts of gonadotrophin in the urine of women at the period of ovulation.

### Discussion

If hyperemia of the rat's ovaries follows injection of the patient's urine in the absence of coitus, and at the period in her menstrual cycle when ovulation might be anticipated, it is postulated that the presence of the hyperemia is an indication that ovulation is occurring. There is no irrefutable proof for this assumption, but accumulating evidence is strongly suggestive.

The positive clinical evidence in support of this hypothesis was the occurrence of conceptions in those women who appeared to be ovulating normally according to the present test; and the negative evidence that women who were not ovulating normally failed to conceive. In the case of one patient, a laparotomy performed on day 2 of the color reaction revealed a 16 mm. follicle, as predicted by the ovulation test previous to the operation.

On the basis of these findings, it might be assumed that ovulation occurs on or within twenty-four hours of the last day of the color reaction.

The experimental evidence in support of the hypothesis is as follows:

The ovulation test is based on the presence of hyperemia in the ovary of the immature rat after injection with the patient's urine. Several pure hormones were tested by the two-hour rat test in effort to establish the cause of the hyperemia. It was found that pure anterior pituitary hormones always produced a hyperemia in the rat ovary. Follicle-stimulating hormone (McShan), luteinizing hormone (Gurin), and follicle-stimulating hormone synergist (Schering) caused color reactions which could be measured differentially by the color scale in doses of from 3 to 25 rat units or equivalent. In doses larger than 25 rat units the maximum five plus color reaction was evident, and it was impossible to grade the increased color by measurement.

Estrogen was the only ovarian hormone that would occasionally cause a color reaction. It is probable that this secondary reaction resulted from the estrogenic stimulation of the pituitary gland, to produce luteinizing hormone, and the subsequent color reaction.

It is a well-known fact that ovulation is dependent upon the hormones from the anterior pituitary gland, namely, follicle-stimulating and luteinizing hormones. Since these hormones cause hyperemia in the immature rat ovary, this evidence suggests that they may be responsible for the hyperemia in the human ovulation test.

The hormone peak for gonadotrophin is an accepted criterion for ovulation, and our findings are in accord with the assay results. However, the assay

method is slow, troublesome, and postovulatory, and the question is raised whether or not ovulation occurs twenty-four hours after the gonadotropic peak.

The postovulatory phase for the subjects with normal reactions (Table III and Fig. 1) averaged twelve to fourteen days for cycles averaging twenty-one to thirty-three days in length. This observation supports the usual understanding that the corpus luteum phase of the menstrual cycle lasts approximately 14 days.

If it can be assumed that the present test can be employed as a means for establishing the time of ovulation, then some of its possible values are as follows:

It will record whether or not, in a given cycle, ovulation has taken place. Thus it will be possible to establish whether a patient ovulates every month and, if not, during just which months it takes place. As a consequence, in the case of couples who are suffering from relative infertility, such information will aid in determining the month during which conception is most likely to occur. Conversely, if it is desired to avoid conception, the tests indicate time when conception is least likely to occur.

Some women showed normal reactions regularly, suggesting that they had ovulated. The evidence for this statement lies in the observation that these patients became pregnant as a result of either coitus or artificial insemination. Other women exhibited some abnormal color reactions during the year, and it is assumed that they did not ovulate normally at those times. The evidence in support of this statement lies in the fact that conceptions never followed abnormal reactions. From these observations, it appears obvious that, should artificial insemination be contemplated, it should not be performed in the absence of a normal color reaction. The color test is of value not only in determining whether artificial insemination should be performed, but also in deciding the day in the cycle when it will be most successful. For example, one patient with cycles averaging twenty-seven days in length, was inseminated for three successive months on days 12 and 14, 13 and 15, 14 and 16 with no success. The two-hour rat test revealed the fact that ovulation had probably occurred on day 9; conception followed insemination performed on day 8 of the following cycle.

One of the chief values of the method lies in the fact that it indicates the beginning of the period of ovulation, which makes it possible to time intercourse for the single day during that period when it is most likely to be fruitful. This selection of the exact day for coitus in relation to ovulation time is important. Pregnancies have resulted in different cases when coitus took place on days 2, 3, or 4 of the color reaction. In most instances, day 3 has been advised. No pregnancies have resulted when coitus took place on the day following the last midperiod color reaction. When the husbands have low spermatozoa counts, it is important to determine whether the color reaction lasts three or four days. Coitus should be advised on the evening of the last day of color reaction. The spermatozoa in such cases probably have a shorter life span than usual, and must be deposited in advance of ovulation.

The success of the test depends upon careful attention to a number of factors. It should be emphasized that a single, tested, strain of animals should be employed. In our preliminary work we observed that certain other strains had ovaries that showed color previous to treatment of any sort, or frequently de-

veloped color through improper technique of handling during asphyxiation, such as failing to turn on the gas immediately, or removing the animal previous to death and replacing it in the chamber. The rats should conform to specific limitations with respect to age and size. Standard lighting conditions for reading the color reaction should be adhered to. If there is any doubt regarding the findings in any subject, the test should be repeated.

### Summary and Conclusions

1. A method is described which appears to indicate (a) whether ovulation is occurring; and (b) when it is occurring.

2. Observations are reported upon 88 married and 12 single women.

3a. Most of these women showed a positive test for three or four successive days each month at the usually accepted ovulation time. This is termed the normal reaction.

b. A few women showed a positive test for one or two days at approximately this same period sometimes followed by a day or more of negative test, then a second positive test for one or two days. This is termed abnormal reaction.

c. A few women failed to show any reaction in any month.

4. Eighteen women complaining of sterility became pregnant during the months when they exhibited normal reactions. These observations suggest that the completion of a normal reaction indicates that ovulation has taken place.

5. Results thus far indicate the third or fourth day of a normal reaction as the time when insemination is most likely to produce pregnancy.

6. In our experience women have not become pregnant in months in which they exhibited no reactions or abnormal ones.

7. Urine assays showed gonadotrophin present when the hyperemic reaction was positive.

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# DELAYED OVULATION, A SIGNIFICANT FACTOR IN THE VARIABILITY OF THE MENSTRUAL CYCLE\*

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SUFFICIENT accurate data on the menstrual cycle have been accumulated to demonstrate that a recurrent 28-day cycle is an abstraction. Deviations occur to such an extent as to indicate clearly that the mechanisms controlling the cycle do not in fact function with an admirable lunar regularity. However much it may appeal to the neat and orderly to think in terms of a 4-week cycle, it is an injustice to the factual data: minor and even major deviations are not necessarily abnormal. Objectivity demands instead that we recognize the innate variability of all biologic processes and search for the causal factors involved. In the present instance this search calls for more complete controls than can be had in the clinic, and leads us to the laboratory and the macaque monkey,<sup>7, 13, 14, 15</sup> a primate whose cycle is essentially similar to the human. In this paper attention will be directed to one type of variation in the menstrual cycle brought about by late ovulation.

The extent to which fluctuations in cycle length occur has had a thorough statistical analysis by Gunn et al.;<sup>11</sup> their study was based on observations that were carefully checked for accuracy, a precaution usually neglected in studies of this sort. Notable exceptions are those of King<sup>17</sup> and Edward Allen.<sup>3</sup> In the group of 979 women studied by the Gunns, only 9 per cent belonged to the extremely regular type with differences of five days or less between the longest and shortest cycles. More than 20 per cent fell outside of the modal group in which cycles averaged 25 to 31 days. It appears that any woman may have an unusually long or short cycle at any time, and the chances that two successive cycles will be of equal length are negligible. A few long-term individual records have been analyzed by Richards<sup>19</sup> and the conclusion is drawn that fluctuations of 1 to 5 days are to be expected in all cases. Since a 28-day cycle occurs only about once in ten times, it is misleading to divide the continuous events of the cycle into 28 stages; the best we can do is to recognize a few phases which, like the entire cycle, are variable.

In order to reduce the inevitable discrepancies between the findings anticipated from the clinical histories and the actual specimens, it has been suggested that the human endometrium be dated from the "expected onset" of the next period rather than from the observed onset of the last. This involves the assumption that the postovulatory phase of the cycle is less variable than the preovulatory, which, in turn, presupposes accurate data on the time of ovulation in the cycle. Hartman<sup>14</sup> has shown how

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unreliable most observations on women are, and has indicated the necessity of using experimental animals for adequate controls. His method of rectal palpation<sup>12, 13, 16</sup> has provided direct and convincing data for the macaque monkey. Having detected ovulation time within a day or two, and knowing the dates of the previous and succeeding periods, he could compare the duration of pre- and postovulatory phases. His two series which total 145 crucial cases checked by laparotomies show that both phases are variable. The postovulatory phase ranged from 6 to 23 days, most cases falling between 9 and 17 days. These findings have been confirmed in principle by Corner.\*

It is to be noted that these observations were made on normal animals in colonies with high fertility records, and that the menstrual flow following each ovulation was actually observed, not computed or estimated. It is accordingly unjustifiable to conclude that ovulation usually occurs at the middle of the cycle simply because the mode of the curve for ovulation time falls between 11 and 14 days, and the modal length of the cycle lies between 26 and 29 days. Ovulation may occur early in a long cycle as well as in a modal cycle or late in a short cycle.<sup>13, 16</sup> So far as the macaque is concerned, the pre- and the postovulatory phases of the cycle vary independently of each other, and their variability is of the same order of magnitude as that of the cycle as a whole.

The irregularity in the postovulatory phase can be readily explained by a finding of Markee.<sup>18</sup> One of the outstanding discoveries in his studies of endometrium transplanted to the anterior chamber of the eye in macaques is the appearance of a profound premenstrual ischaemia. This preceded extravasation in every one of the 432 cycles he studied, and it always involved a reduction in the size of the transplant. The ischaemia varied both in duration and intensity, appearing as much as five days before the onset of bleeding or only one day before. If we correlate the ischaemia with the decline of activity in the corpus luteum, it would seem that this organ in the absence of pregnancy may "fail" suddenly and completely or only very gradually.

The ischaemic phase can readily be recognized histologically, and its variable duration can be correlated with the extremely variable histologic picture presented by the menstruating endometrium after ovulatory cycles. Thus, on day 1 the endometrium may be only 2 mm. thick, in areas where the surface is still intact, or it may be 6.7 mm. The glands may be "progravid" or narrow and simple in form. This statement is based on the study of 46 menstruating macaque uteri with complete histories and ovarian data from the collections of Corner, Hartman, Van Dyke, and Bartelmez. It is probable that similar conditions obtain in the human species where similar differences are found in menstruating mucous membranes.<sup>4</sup>

When and if a fully reliable external sign of ovulation in women is discovered, we will be in a position to gather data and judge to what extent the two species agree as to the relations of pre- and postovulatory phases.<sup>14</sup> It is not likely that there will be any fundamental differences.

\*Contrib. to Embryol. 31: 117, 1945.



The present report is concerned with certain evidence provided by the macaque on the preovulatory phase of the cycle. Markee<sup>18</sup> states that after the end of a menstrual period the flow of blood and the growth of endometrial transplants may be promptly accelerated, or there may be a postmenstrual "resting" period lasting up to ten days. We have observed postmenstrual phases lasting much longer. They showed little evidence of endocrine activity. These occurred during the breeding season in normal, active macaques. The evidence appears in the following protocols.\* The data on sex skin are included because when changes in color can be observed, they usually indicate changes in blood estrin.<sup>1</sup> The doubt that has been cast on their validity is due largely to the fact that the changes may not be apparent to the eye, though they are revealed when matched against color scales.

CASE 1.—(H314) This macaque, who had been notably regular in her cycles, menstruated from February 19 to February 23. The sex skin became strikingly paler during menstruation, and it remained pale for three weeks. On March 12 (day 22 of the cycle), the color began to brighten, and daily rectal palpations were done. On March 21 (30 days after the previous onset) ovulation occurred. Seventeen days later, on April 7 (day 48), a menstrual period began. This occurred 26 days after the return of ovarian activity as judged by changes in color of sex skin. The animal was sacrificed and the endometrium showed a typical ovulatory menstruation. The diagnosis made by G. W. Corner on the corpus luteum of the right ovary was "early degeneration as in menstruation."

CASE 2.—(B326) The January cycle was 25 days in length. It was anovulatory according to the palpation findings. The February flow persisted for 6 days. The sex skin color remained pale, and on day 13 both ovaries were small. On day 19 the color rose, but both ovaries were still small and remained so until day 25, when the right ovary began to enlarge. The color remained high, and on day 29 this ovary was definitely smaller and softer, indicating that ovulation had occurred on day 28. On day 32 the right ovary had again become larger, and on day 35 the animal was killed. The corpus luteum was 6 to 7 days old, and the endometrium presented an early pro gravid picture.

CASE 3.—(B318) The October cycle lasted 23 days; that in November, 22 days; and in December, 23 days. A menstrual period had begun on December 31 and ended January 2. Palpation on day 10 of the cycle indicated an enlarged ovary, so the animal was mated. On day 14 this ovary was definitely smaller, but it remained small, and neither pregnancy nor menstruation followed. This suggests the development in January of a Graafian follicle which became cystic and then slowly disappeared. The change in hormone level was presumably not abrupt enough to bring about menstruation.<sup>18†</sup> On day 23 the right ovary had again enlarged, and ovulation was diagnosed between days 29 and 30. When the animal was sacrificed on day 42, a mature corpus luteum was found on the right. The endometrium presents the first signs of the premenstrual ischemic phase, so that menstruation was imminent.

CASE 4.—(B317) In October ovulation was diagnosed on day 22, and the next flow appeared 16 days later (38-day cycle). During the postmenstrual phase, the sex skin color remained consistently high (Tallquist hemoglobinometer rating 60). The next ovulation was diagnosed between days 36 and 37, and on day 41 a fresh corpus luteum was observed at laparotomy. Fifteen or 16 days after ovulation (day 52), menstruation began and both corpus luteum and endometrium presented histologic pictures typical of early menstruation.

\*We wish to express our indebtedness to Dr. David B. Clark for help in making these observations.

†This type of abortive cycle was first described by Hartman<sup>12</sup> (Staircase phenomenon) and probably accounts for many cycles which are about twice the modal length.

TABLE I. CASES WITH LONG POSTMENSTRUAL PERIODS OF OVARIAN INACTIVITY (MACAQUE)

NO.	DAY OF OVULATION AFTER ONSET OF PREVIOUS MENSTRUATION	TOTAL LENGTH OF CYCLE IN DAYS	AVERAGE OF PREVIOUS CYCLES	REMARKS
I (B314)	30	48 (Feb.-Mar.)	26 (range 24 to 28)	Postovulatory phase, 18 days
II (B318)	29 or 30	Estimated 43 (Jan.)	32 days (range 22 to 58)	Premenstrual isehemic endometrium
III (B317)	36 or 37	52 (Nov.-Dec.)	28 days (range 22 to 45)	Menstruation 15 to 16 days after ovulation
IV (B326)	29	Estimated 42± (Mar.)	25 days (only one cycle observed)	6-day-old corpus luteum obtained on day 35. See the similar case 94 of Brewer and Jones <sup>6</sup>
V (B211)	21 to 23	Estimated 36± (Dec.)	41 days (range 25 to 60)	Panhysterectomy on day 27. Corpus luteum 4 to 6 days old
VI (H376)	26	Estimated 41± (Oct.)	Previous eyele ovulatory	Newly ruptured folliole and follicular phase endometrium removed on day 26

CASE 5.—(B211) A menstrual period lasted from December 16 to 21. Both ovaries were small on days 13 and 16 of this cycle. On day 21 the left ovary was found enlarged, and on day 23 recent stigmas were observed in both ovaries at an exploratory laparotomy. On day 27 a panhysterectomy was done and each ovary had a corpus luteum estimated as 4 to 6 days old by Dr. Corner.

CASE 6.—This case was added to Table I with the permission of Dr. Hartman. It is as clear a demonstration of normal ovulation during the fourth week of a cycle as could be wished.

These specimens show no evidences of abnormality in either uterus or ovaries. Four of them were collected in a single season from a colony of some 30 mature animals. In the Corner, Hartman, and Van Dyke collections, there are at least six long preovulatory phases; in two, ovulation was demonstrated on days 17 and 23, respectively;<sup>13, 16</sup> in four no ovulation had as yet occurred on days 17, 17, 19, and 24. These might have belonged to anovulatory cycles, but numerous mitoses in the endometrium suggest that ovarian activity had been resumed and that ovulatory cycles had begun. It would seem then that in the macaque, delayed ovulation is not rare.

There are reasons for believing that delayed ovulation also occurs in women. The most convincing are to be found in Hartman's<sup>14</sup> review of normal early pregnancies with exceptionally reliable clinical histories. In 18 of the 54, that is, one-third, ovulation occurred between the 18th and 24th days of the cycle. In a group of 30 women with normal pelvic organs reported by Greulich, Morris, and Black,<sup>10</sup> there were no large follicles or corpora lutea present in fourteen examined at laparotomy between days 13 and 19. Brewer and Jones<sup>6</sup> report a 5-day-old corpus luteum (case 94) removed 38 days after the last period. In Fluhmann's<sup>9</sup> study of cycle length, 10.5 per cent of 747 cycles fell between 36 and 50 days. Some of these could be ascribed to delayed ovulation, if anovula-

tory cycles are as rare in women as we are led to believe. Others might be cases with a long-lived corpus luteum such as Hartman<sup>10</sup> has described.

Instances of ovulation have been adduced for every day of the conventional 28, and it has accordingly been argued that ovulation has no definite locus in the cycle, but may occur at any time. Many of the "aberrant" cases can be accounted for by delayed ovulation. Thus, if the postmenstrual inactive phase varies in duration, the subsequent ovulation may occur on any day of the third or fourth week after the last observed menstrual flow. The rare cases of ovulation during or immediately after bleeding can be explained on the same basis. If there is a latent period of three weeks or more, and the return of ovarian activity is followed by the ovulatory (intermenstrual) type of bleeding,<sup>12</sup> this might readily be misinterpreted as a light menstruation, and consequently a follicle be supposed to have ruptured during the catamenia. Variability in the time of ovulation is no good reason then for questioning the causal relationship between the various events of the menstrual cycle.

All the information we have at present indicates an infertile period in women, but only *statistically*.<sup>2, 5, 14, 20</sup> A woman who requests advice on this subject may ask, "What are the chances in my case that an ovulation will occur three or more weeks after a period?" There is no pat answer, even if she has kept a menstrual calendar for years. Many "failures of the safe period" can be ascribed to our ignorance of the incidence of delayed ovulation in women. There are 16 cases which can be so interpreted in our Culbertson Collection of human endometria from 300 successive hysterectomies.

Gunn, Jenkin, and Gunn<sup>11</sup> have pointed out that the variability in cycle length is like that of any character which is determined by many diverse factors. Variability in the pre- and postovulatory phases is to be expected if they are controlled by an oscillating system of balanced endocrine forces. As in the parallelogram of forces, the configuration of such a system as a whole is necessarily modified by every change in any one of the component forces. We are dealing not with a machine of levers and gears, but with a system of living organs. The activities and susceptibilities of one or more may change from month to month and, as a result, the time relations vary. The resultant state of a "target organ" like the uterus also varies. There is no reason for regarding the postmenstrual periods of ovarian inactivity as abnormal. They are integral features of the variability of the preovulatory phase and should be considered as comparable with the quiescent (anestrus) periods such as characterize the reproductive cycles of most mammals.

### Summary

The pre- and postovulatory phases of the menstrual cycle are as variable in length as the cycle as a whole in the macaque (Hartman).

Such variability can readily be explained in a cycle controlled by a balanced system of endocrine forces.

Ovulation is demonstrated on the 21st to the 23rd, 29th, 29th to the 30th, 30th, and 36th days after the onset of normal menstrual periods in a colony

of healthy, mature macaques. There is evidence that such delayed ovulation occurs more frequently than these five crucial cases would indicate.

Delayed ovulation in these cases was due to a postmenstrual period of ovarian inactivity.

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## SEMEN ANALYSIS IN 1,500 CASES OF STERILE MARRIAGE\*

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DURING the past few years at the New York Hospital and Cornell University Medical College, we have examined approximately 1,500 semen specimens obtained from different individuals whose wives were undergoing examination for sterility either in the clinics of the hospital or in the offices of private physicians. We believe that the results of these semen analyses have considerable value, inasmuch as the tendency in recent years has been to apportion more blame to the husband in sterile marriage. This shift in emphasis is due in great part to increasing knowledge of the physiology of human semen, particularly from the work of Cary,<sup>1</sup> Moench,<sup>2</sup> Hotchkiss,<sup>3</sup> Williams,<sup>4</sup> and others. A gradual accumulation of data has drawn attention to the significance of the spermatozoa count, the motile activity of the spermatozoa, and the morphologic characteristics of the cells. In spite of the evolution of such standards, there is still considerable debate about the relative significance of each characteristic of the semen. One group of opinion considers that abnormal spermatozoa morphology is of prime importance; another the spermatozoa count per unit volume, while yet another is content to view the semen specimen as a whole and to judge its potential fertility on a broad basis.

We believe that the latter approach is the logical one, though it is obvious that no real conclusion can be reached until the histories of both partners in sterile marriage are studied intensively and a mass of statistical data obtained which will allow us to apportion the responsibility more adequately than we can at present. We require, particularly, more knowledge of what can be expected of semen specimens from apparently normal young men in the age group of 20 to 35, and to compare such figures with the data to be presented here, namely, the characteristics of the semen of men in sterile marriage. In this and other related studies, we hope to present data which will throw more light on a problem which is assuming increasing importance.

### Methods

The semen specimens were obtained at least three days, preferably longer, after the last emission. The patients were supplied with a clean, wide-mouthed glass container and instructed to obtain the specimen by masturbation if possible; if not, then by interrupted intercourse.‡ They were cautioned against losing any of the first part of the ejaculate, since it has been shown<sup>5</sup> that most of the spermatozoa appear in the first third of the ejaculate and that the motility of the spermatozoa in the terminal portion is likely to be impaired.

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†Dr. Hotchkiss is now in service in the U. S. Navy.

‡It should not be necessary to emphasize that a condom specimen is likely to prove grossly misleading inasmuch as motility is badly impaired or destroyed by such a method of collection.

The semen specimens were brought to the laboratory within two hours after ejaculation and examined immediately for volume, the quality of motility, and the percentage of active spermatozoa. The motility determinations were done according to the method of Hotchkiss.<sup>3</sup> It should be noted that this method gives separately an appraisal of the quality of motility and the percentage of active cells.\* In a normal specimen, full active should be maintained for at least three hours. Motility determinations were made at three, six, nine, and twenty-four hours. Any abnormality in viscosity was noted when the volume was taken.

In counting the spermatozoa, the technique described by Macomber and Saunders<sup>6</sup> was followed.

The morphology of the spermatozoa was studied by the method and using the criteria of Hotchkiss.<sup>3</sup> Where possible, three hundred spermatozoa were examined, though in many specimens with low counts this was not feasible. We also have found the staining technique of Greenberg et al.<sup>7</sup> to be valuable in these studies, particularly since with this method a stained smear ready for study can be obtained in two minutes.

Under the heading "poor motility" we have grouped semen specimens in which the motile activity of the spermatozoa was less than a quality of three and/or where only 40 per cent or less of the spermatozoa were active. This type of motility is decidedly subnormal.

In grading the morphologic characteristics, we have placed the normal limit as under 20 per cent abnormal forms, and characterized all semen specimens with 20 per cent or more abnormal forms in the subnormal class. This does not imply that the latter semen specimens necessarily are infertile but only that, so far as morphology is concerned, they are considerably below the average normal semen specimen (MacLeod and Heim,<sup>8</sup> and Moench and Holt).<sup>2</sup>

### Details of Semen Analysis

The figures in Table I present a characteristic of the semen analysis which hitherto has not received much, if any, emphasis. It will be seen that as the spermatozoa count falls, other defects in the semen increase almost in proportion. For example, in the presence of counts of 100 million per c.c. or more,

TABLE I. SEMEN ANALYSIS IN 1500 CASES OF STERILE MARRIAGE

SPERMATOZOA COUNT/C.C. IN MILLIONS	NO. OF CASES	SUBNORMAL MOTILITY (3- OR LESS AND/OR LESS THAN 40% MOTILE)	SUB- NORMAL MORPHOL- OGY (20% OR MORE AB- NORMAL)	SUB- NORMAL MOTILITY AND MORPHOL- OGY	SUB- NORMAL MORPHOL- OGY WITH GOOD MOTILITY	NUMBER POOR NOT CONSIDER- ING COUNT	SATISFAC- TORY SPECI- MENS*
100+	453	103 (24%)	41 (9%)	28	13	116 (25%)	337 (74%)
80-99	117	25 (21%)	18 (10%)	8	10	35 (30%)	82 (70%)
60-79	156	56 (36%)	20 (13%)	13	7	63 (40%)	93 (60%)
40-59	171	76 (45%)	52 (32%)	36	16	92 (54%)	
20-39	175	117 (67%)	58 (33%)	35	22	139 (79%)	
1-19	272	221 (81%)	?				
Azoospermia	156						

\*Of 1,500 semen specimens, only 512 (40%) were completely satisfactory.

\*Appraisal of quality is a matter of experience. Speedy and undeviating progress across the high power microscopic field is the prime requisite of normal motility.

25 per cent of these specimens were poor in terms of motility and morphology and poor, therefore, in terms of potential fertility. In specimens with counts between 80 and 100 million per c.c., 30 per cent were unsatisfactory for the same reasons, not a significant increase. However, in the 40 to 60 million per c.c. class, defects apart from the count rise to 54 per cent, and in the 1 to 20 million group at least 81 per cent of the specimens are deficient in both motility and morphology. In most of the latter cases, we were not able to do adequate morphologic examinations because of the sparsity of cells and we believe, therefore, that a percentage of 90 would better represent the number of specimens deficient for reasons other than count. Fig. 1 demonstrates in graphic fashion the increase in other defects with decrease in counts.

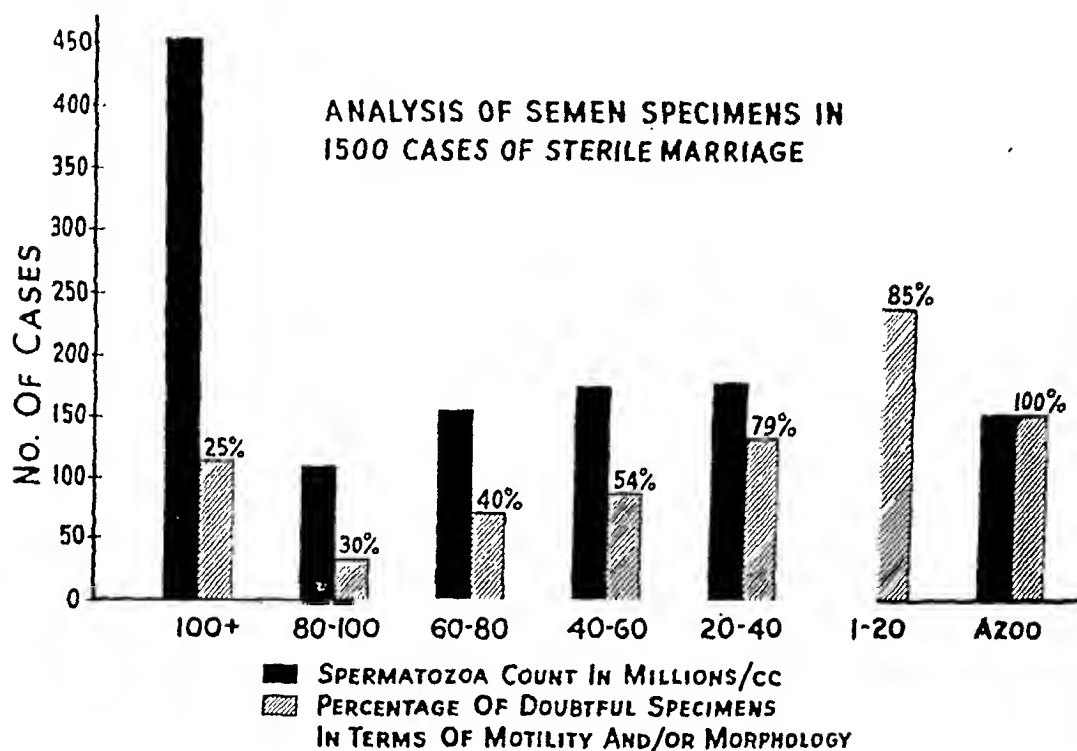


Fig. 1.

These figures have considerable value in displaying what might be expected of semen specimens in sterile marriage. But their greatest interest and worth derives from a comparison of this data with those obtained from men of known fertility and from apparently normal young men. Hotchkiss et al<sup>9</sup> have published figures obtained from 200 fertile men whose wives were in the first half of gestation, and MacLeod and Heim<sup>8</sup> give data from apparently normal young men. Table II summarizes and compares the figures for volume, spermatozoa count, and morphology of the three different groups.

TABLE II. SUMMARY OF SEMEN QUALITY IN VARIOUS MALE GROUPS

AUTHOR AND GROUP	VOLUME OF EJACULATE (C.C.)	SPERMATOCYTES COUNT IN MILLIONS/ C.C.	TOTAL SPERMATOCYTES COUNT IN MILLIONS	MORPHOLOGY % OF NORMAL FORMS
Hotchkiss et al. (Fertile Marriage)	3.0	120.5	360	89.8
MacLeod and Hotchkiss (Sterile Marriage)	3.2	94	277	87.0
MacLeod and Heim (Unmarried Men)	3.4	134	435	90.0

The average volume of the ejaculate is quite similar in all three studies. Generally speaking, we found negligibly few cases in which low volume could be considered as the source of infertility.

The average spermatozoa count per c.e. and total count show all three groups to be satisfactory by present standards. It should be noted (Table I) that 10 per cent of the "sterile marriage" group were azoospermias. In calculating the mean spermatozoa counts in this group we have not included the azoospermias, so that the average counts presented represent only those semen specimens with spermatozoa present. In spite of this allowance, the average spermatozoa counts of this group are considerably, but not seriously, lower than the others. The highest counts are found in the unmarried group, but when compared to the "known fertility" group, the difference is not unduly significant. In other words, looking broadly at the average figures of all three groups, the average spermatozoa count in the husbands of the "sterile marriage" group is satisfactory, if not good, by present standards. Similarly, one can find no significant difference in the average percentage of spermatozoa of normal structure in the three groups. Therefore, in considering these two characteristics of the semen, the average figures do not indicate the true state of affairs. It is rather in the count distribution that significance appears. For example, if we take the 60 million per c.e. count level arbitrarily as the point of demarcation, it has been shown<sup>9</sup> that 25 per cent of a group of men of known fertility had counts below this level. Similarly,<sup>8</sup> only 22 per cent of a group of apparently young men had counts below 60 million per cubic centimeter. Whereas, in the sterile marriage group, 49 per cent of the semen specimens were in the lower count brackets.

It is generally agreed<sup>6, 10</sup> that the best chances of conception are found in specimens with counts of 100 million per c.e. or over. Thus, in the group of fertile men, Hotchkiss et al.<sup>9</sup> found that 60 per cent of their men fell in this category, and MacLeod and Heim<sup>8</sup> found 65 per cent of the men in their younger age group had counts of 100 million per c.e. or over, a rather striking difference.

Simmons,<sup>11\*</sup> in a recent study of the semen in 500 men in sterile marriage, has data which corresponds very closely with the figures presented here. Using essentially the same techniques and standards, he found, for example, that 47 per cent (we found 49 per cent) of his semen specimens had spermatozoa counts below 60 million per c.e. Semen specimens with 100 million per c.e. or over comprised 37 per cent in his group as compared to 30 per cent in our group. Taking all the characteristics of the semen, Simmons finds that only 40 per cent of the males in his group had satisfactory semen specimens, a figure which coincides exactly with ours. It should be pointed out, however, that Simmons and we found specimens unsatisfactory for different reasons. Simmons places considerably more emphasis on defects in morphology in that he found 28 per cent of the total number of specimens examined to have defective morphology, while we have classified as such only 18 per cent. Inasmuch as we have used the same figure (20 per cent or more abnormal forms) as the point at which to consider a specimen as having subnormal morphology, it is obvious that Simmons uses more rigid criteria in characterizing a spermatozoon as normal or abnormal. Similarly, in regard to motility, our standards must be different in that 35 per cent of our total number of cases were considered defective in motility, whereas Simmons found only 20 per cent. So that, although we obtain the same percentage of unsatisfactory specimens, we do so in certain instances for different reasons.

Keshin and Pinck,<sup>12</sup> in a study of 135 cases of men in sterile marriage, consider that 68 per cent of the semen specimens examined were unsatisfactory, a

\*I am deeply indebted to Dr. Simmons for the privilege of reading his manuscript while his paper was in press.



very high figure indeed. They, like Simmons, considered abnormal morphology a more serious problem than subnormal motility, so much so that 25 per cent of their total series are classified as defective because of abnormal morphology.

### Azoospermia

In his 536 cases, Simmons found that 71 (13 per cent) were azoospermias. But, of 135 cases, Keshin and Pinck had a total of 25 (18.5 per cent). We found 156 cases (10 per cent) in our group, though the percentage figure is higher (15 per cent) if we consider only cases seen in the hospital clinics. Gonorrhea is considered in most texts as the most common cause of sterility in the male, but Simmons points out that in only 18 of his 71 cases of azospermia was gonorrheal epididymitis the probable cause of the sterility. Keshin and Pinck do not subclassify their cases. Our case histories are not complete because, in many cases, testicular biopsy, the only confirmatory measure, was refused. However, if we take only the clinic cases, of which we have 577, 88 were definitely azoospermias. Of the 88 cases, 50 (or 56 per cent) had a history of gonorrhea, 29 were either hypogonads or cases of bilateral cryptorchidism, and nine were of obscure etiology. Thus, in our clinic cases, the percentage of azoospermias with a history of gonorrhea is rather high, though the lack of testicular biopsy in most of these cases makes the evidence that gonorrhea is the cause of the sterility only presumptive. There is little doubt that a number of these cases would have had poor semen specimens in the absence of the gonorrhea history or bilateral obstruction. It is equally true, however, that the probability of a congenital azoospermia being found in the presence of bilateral obstruction due to gonorrhea is not high. It is of interest to note that a much higher percentage of cases of azoospermia are found in our clinic cases (15 per cent) than in the private patient group (7 per cent). It is also true that histories of gonorrhea are much more frequent in the clinic group. We agree with Simmons that, taking the male population as a whole, gonorrheal epididymitis is not the most common causative factor in azoospermia, though it might well be so in restricted groups.

### Relation Between Abnormal Semen Viscosity and Sperm Motility

Abnormally high viscosity is a frequent finding in examinations of the seminal fluid, and it is pertinent to ask if subnormal motility is correlated with such a finding. Our evidence suggests that there is no such correlation. For example, in 500 individual examinations, 50 specimens were found with a marked increase in viscosity. Of these specimens, 24 had spermatozoa counts above 60 million per c.c. and, of these, only three had unsatisfactory motility. We have already shown that, apart from the viscosity factor, motility defects increase markedly when the count falls below 60 million. It would seem, therefore, that if the spermatozoa are intrinsically good so far as motility is concerned, an abnormally viscous seminal fluid is not likely to affect that quality.

Insofar as the ultimate functioning of highly viscous semen in the female genital tract is concerned, we believe that if the *in vitro* quality of the sperm motility is good, the spermatozoa will migrate from viscous semen into the cervical canal just as readily as from semen of normal viscosity.

### Type of Semen Specimen Eventually Producing Conception

In the sterile marriage group reported here, we have complete histories on 140 cases in which 24 pregnancies eventually took place. Undoubtedly, many others have resulted which are not reported either to the clinic or the private physician. Of those recorded, we have complete histories on the husband and wife and it is of considerable interest to examine the data, particularly in

TABLE III. ANALYSIS OF 142 HISTORIES OF BOTH PARTNERS IN STERILE MARRIAGE

BOTH HISTORIES GOOD	WIFE'S HISTORY GOOD HUSBAND'S POOR	HUSBAND'S* HISTORY GOOD WIFE'S POOR	BOTH HISTORIES POOR	SUBSEQUENT PREGNANCIES
34	43	28	14	25

Of 25 pregnancies which occurred subsequently in this group:

- 16 (or 54%) took place where histories of both partners were good.
- 7 (or 28%) took place where wife's history was good and husband's semen was poor.†
- 1 occurred where husband's history was good and wife's poor.
- 1 took place in presence of poor histories in both partners.

\*Semen specimens of husbands averaged 127 million spermatozoa/c.c.

†In these cases the count details of the semen specimens are:

	1.	2.	3.	4.	5.	6.	7.
Millions/c.c.	5	26	20	23	50	45	48

terms of the semen specimen. Table III gives the number of pregnancies occurring in the different history categories. At the time of original examination, the average number of years of infertility was 2.6. Conception eventually took place in these cases sometimes two to three years after initial examination, so that the years of infertility really average higher than 2.6.

Where the husband's semen specimen was unsatisfactory on the initial examination at least another one, and in many cases 3 or 4, repeat tests were done. The male partner was considered of low fertility when the spermatozoa count was consistently below 60 million per c.c. or other defects, such as in motility or morphology, were obvious.

It will be seen that the greatest number of pregnancies (60 per cent) occurred eventually in cases where no fault could be found in the wife and where the husband's specimen was good. So far as this report is concerned, the average figures for these semen specimens are significant. The spermatozoa count averaged 127 million per c.c. (low 62 million, high 220 million), the motility in every case was good, and the normal forms averaged 90 per cent.

In only one other history category did a number of pregnancies (7, or 29 per cent) eventually result, namely, where the wife's history was good and the husband's relatively poor. The average figures for the semen specimens of these husbands are 31 million per c.c. (high 50 million, low 5 million). In at least three of these cases the motility, too, was subnormal.

It is obvious from these results that one cannot arbitrarily forecast the fertility of any semen specimen provided spermatozoa are present. Nevertheless, it is just as obvious (and perhaps axiomatic) that the chances of conception are considerably better when the spermatozoa count is in the count level above 60 million per c.c. This fact is brought out strikingly when we see that where the histories of both partners were good, pregnancies eventually resulted in 15 (or 65 per cent) of the cases. Whereas, where the wife's history was good and the husband's poor, pregnancies eventually occurred in 7 (or 16 per cent) of the cases.

It is of interest, too, to point out that in 28 cases where the semen specimens were good but the wife's history poor for one reason or another, only one pregnancy eventually took place. It would seem, therefore, that if the wife's history is good, the chances of conception eventually taking place are reasonably good (one in six) even though the husband's semen specimen does not measure up to normal standards. One normal pregnancy eventually resulted in the latter group from a semen specimen which contained only 24 per cent normal spermatozoa—64 per cent of the spermatozoa being of the "tapering" type, classified by most authorities as abnormal.

### Abnormal Morphology

Throughout this analysis we have found no convincing evidence that a high percentage of abnormally-shaped spermatozoa in any given semen specimen was the *sole* responsible factor. We have isolated cases on record where, in the presence of a good spermatozoa count and adequate motility, the morphology has been grossly abnormal in the sense that only about 10 per cent of the spermatozoa showed normal structure. But such cases are rare, and when they occur we have little hesitancy in ascribing the failure of conception to this one factor. But, as we believe the figures show, one defect in the semen specimen is usually accompanied by others, hence our reluctance to single out abnormal morphology as a serious, *single* factor in male infertility.

### Discussion

One of the significant features of the data presented here is that in this large series of cases, so many semen specimens are defective by present standards. If we compare these figures with apparently normal standards in the literature we find, for example, that in a group of 200 men of known fertility, 25 per cent were found to have semen specimens with counts consistently below 60 million per c.c.<sup>9</sup> In another group of 100 apparently normal, young, unmarried men, the average spermatozoa counts were just slightly higher than those given for fertile, married men, and 22 per cent had spermatozoa counts consistently below 60 million.<sup>8</sup> In these two groups, therefore, the average semen characteristics were surprisingly similar. We have shown in this sterile marriage series that the average semen characteristics are considerably below the level of the two groups referred to above though the average figures are still acceptable. However, more than 50 per cent of the semen specimens examined had spermatozoa counts below 60 million per c.c. as compared to 25 and 22 per cent in the normal groups. Six hundred and eighteen, or 41 per cent, of the total number of men examined had subnormal spermatozoa counts; and it is in this group, not the completely sterile group with azoospermia, which constitutes the main male sterility problem. Most of these men have normal histories. Except in certain of the azoospermias, no clean-cut etiologic factor (or factors) has emerged to account for the considerable amount of male infertility recorded in this investigation.

### Summary

1. Examination of semen specimens in 1,500 cases of sterile marriage showed that about 50 per cent had deficiencies either in spermatozoa count, motility, or morphology.

2. As the spermatozoa count falls below 60 million per c.c., other defects, such as motility and abnormal morphology, become more apparent until, in the very low count range, all three deficiencies together are likely to be found.

3. Where successful pregnancies eventually occurred in this large group, the greatest number were found where no obvious fault was apparent in either partner and where the spermatozoa count was consistently in the higher brackets.

4. It is suggested that the 60 million per c.c. spermatozoa count level is a reasonable dividing line between good and impaired fertility.

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## WEIGHT CONTROL, DIET, AND FLUID BALANCE IN PREGNANCY\*

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THROUGH years of experience in a chosen type of work, one begins to evolve for oneself a pattern of what he believes is the proper course to pursue to secure an ideal end result. From observation and experience, we unconsciously set a routine that strikes us as meeting this criterion. In many instances, self-evident facts and procedures of worth are overshadowed by the more spectacular discoveries of modern times. A new extraperitoneal approach to the lower uterine segment, or a new wonder drug, overcomes a serious obstacle to success, and the old time-worn procedures are allowed to pass unnoticed, especially if they lack the glamour of the spectacular. By this indifference to simple things, we often produce the difficulties that the newer things were invented or discovered to correct.

It is felt here, for example, that the proper control of the diet, weight, sodium-ion intake, and the proper supply of vitamin foods and adjuvants, plus exercise, are extremely important. These factors are, in themselves possibly, the very basis for the prevention of so-called "toxemia" of pregnancy and can reduce the incidence of dystocia.

For years we have been impressed with several self-evident facts. (1) While not every woman gaining weight excessively gets into trouble, the greatest number of those who develop toxemia or dystocia do gain inordinately. Very possibly, these difficulties are due to this fact. (2) The patient who gains little weight usually has a shorter labor and much less obstetric complication.<sup>1</sup> (3) Efforts to control weight in order to lessen the size of the baby have repeatedly been failures; so in reverse, patients may be dieted without any appreciable effect on the size of the baby.<sup>2</sup> (4) The offspring of women in privation are no smaller or poorer than the offspring of their more fortunate sisters; in fact, they are often more rugged. The baby is, after all, a parasite. (5) The generally accepted fact that pregnant women need far more protein than normal in order to protect their liver and to maintain proper blood serum protein is true. (6) The excellent results that have accrued through the real enforcement of fluid balance and restriction, and especially dehydration in their proper place, are accepted in this institution.<sup>3</sup> (7) The importance of exercise is conceded as important to proper body function. (8) The effect on the woman herself is very important. It is the nature of woman to be the attractor, and, whether married or not, she instinctively desires the utmost in the physical perfection with which she was originally endowed. Any obstetrician who allows a woman to lose her attractiveness is depriving her of many things that make for her mental well-being, her husband's contentment, and her own personal satisfaction. There is nothing

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more satisfying than the gratitude of the woman who has been carried through her gravid state and is as well and as attractive as she was before. We have been successful, in all patients who have been willing to cooperate with us, in having the weight the same as when they started, or the difference of a pound or two either way.

After the appearance in *Surgery, Gynecology and Obstetrics*, August, 1932, of the paper by Arnold and Fay<sup>3,4</sup> of Temple University, Philadelphia, describing the so-called "Temple Treatment" of eclampsia, the Obstetrical Department of St. Mary's Hospital as then constituted, and in conjunction with the medical department, decided to evaluate the results in our, then, relatively frequent eclamptic cases. The results were so striking that it was reasoned that if this could and does cure, prophylactically, it should prevent all the symptom complex. Again, many observers have suggested the importance of sheer weight as a factor in "toxemia."

With these thoughts in mind, it was decided several years ago to enforce a strict regimen on private patients. The reasons are carefully pointed out to them, namely: the dangers of excessive weight; the possibility of long, hard labor; the possibility of "toxemia"; the desirability of maintaining physical appearance after the gravid state is ended; the comfort that these persons have while they are pregnant; and the ease of accomplishing normal activities. They are, of course, in the beginning extremely enthusiastic, and many carry on willingly, faithfully, and get the desired result. Others—the spoiled ones—usually gain weight, rebel, and it is only by threats and their husbands' help, that we are able to make them toe the mark. As a result, all of these women, even the rebels, are delighted with the result.

In order to evaluate properly this regimen, I have taken 325 consecutive cases that have passed through my office and have been subject to this method of treatment. Not included were patients seen in consultation at the hospitals and patients referred in the last minute without data. There were some patients referred by doctors who have gone into the service, and others who have come in mid-pregnancy and who had already gained weight excessively. These latter were included and are the source of most all of the heavy gains. There were several who came to see me after therapeutic abortion had been advised for hypertensive vascular disease, heart disease, etc.

In the beginning the weight allowance was 20 pounds, and later it was reduced to 15 pounds as the top weight gain for the average woman; but, the larger the woman, the less the gain allowed, and for the unfortunate obese, the ideal was no gain whatsoever.

### Procedure

After the general instructions to the patient as to what is expected of her and the results that she may expect from complete cooperation, she is given the usual complete medical and obstetric examination. The proper diet is stressed and she is told how to provide herself with the proper food intake. Here, this means a high protein diet, that is, protein ingested three times a day, which is supplemented by a diet that is low in carbohydrate, high in green and yellow vegetables, fruit, and certified milk, either skimmed or whole, as the diet in-

dictates. In this way, sufficient protein is ingested, sufficient vitamins and salts are included, and carbohydrate is provided in sufficient amount through the ingestion of the vegetables and fruit. All of the heavy starches are absolutely eliminated until we find just what the woman's food requirement is. This must be determined because many women can eat enormous quantities of food in the nonpregnant state without gaining a pound, but pregnancy produces a tremendous gain which must be controlled. Added vitamins are provided and, by frequent office visits, her weight is maintained so that in her first four or five months she is permitted only a maximum gain of one-fourth pound per week, and if she is obese, she is permitted no gain at all. This early diet regulation is important because in the latter months of pregnancy, as the woman becomes more sedentary, she is apt to put on excessive weight. This is not readily controlled because the restriction in diet has not been started early enough. The patient is seen at least every three weeks at first and, if she is a diet problem, every week until she strikes a proper average. These patients, if gaining beyond their allowance, are put on a 1,200 calorie diet plus added vitamins, which is almost exclusively protein and largely vegetable. More food is later added, and her total caloric requirement found so that she will gain the allowed progressive amount. Salt is not restricted in the early months, except the ingestion of highly seasoned things, and the excessive use of salt is forbidden. Later, salt is permitted only in the preparation of food. Fluids are important. The woman who can metabolize water is, of course, the usual type. In pregnancy, however, women's water metabolism is notoriously unsatisfactory, and patients are repeatedly checked as to the amount of fluid they take against the amount of urine they excrete. If there is a sudden weight gain the fluid balance is checked. This is done especially in the woman who has been gaining satisfactorily and suddenly shows a pound or more gain, with or without transient edema. This means that she must at intervals measure her intake and output. Her fluid intake is *restricted to her previous day's output*. The salt is withdrawn and, if her fluid intake and output does not satisfactorily balance, she is instructed to take magnesium sulfate every morning to produce free fluid evacuation. I have never seen any harm from this procedure, and these patients themselves remark how well they feel. It is surprising the amount of fluid these patients can lose, as evidenced by weight loss. Their intake is then increased, and if they are able to metabolize a fair amount of fluid, it is allowed, and a balance struck which seems to be best for them. It is also amazing how comfortable they are, how the lassitude disappears, and, what is more important, how often they will ask to be put back on this routine because they feel so much better. In passing, no patient is allowed to take less than 20 ounces of fluid a day. This, of course, does not mean water allowance alone, but means water in any form, such as tea, soup, milk, or other liquid. One thing we must always watch for carefully is edema, which becomes marked or persistent in spite of this routine. Patients with edema usually belong in either one of two groups: they either eat little protein, or they are heavy protein eaters when not pregnant, and require a great deal more when gravid. Either one of these may get a simple nutritional edema which is alarming unless properly evaluated; also, this may be the first evidence of liver dysfunction. This type of patient persists in having edema beyond a few days, which is not markedly relieved by dehydration. She balances well and has no other evidence of damage; for example, rise in blood pressure, or albuminuria. These patients are hospitalized to make sure that they are maintaining the proper regimen. Almost invariably we find a severe hypoproteinemia. The serum-albumin and serum-globulin ratio is reversed and the serum-albumin is below two. These patients, of course, are headed for trouble. It is not known at this stage, whether their hypoproteinemia is an evidence of liver damage or dysfunction, and is thus an early stage of toxic disease, or

whether it is simply some type of nutritional or ideopathic edema, but it calls for immediate control. These patients are put on a very high protein diet supplemented with hydrolysate of protein, and are given an infusion of whole plasma (500 c.e.) by vein. This is not the ordinary plasma which is used in shock. Our blood bank prepares this pooled plasma just for this purpose. In ordinary plasma for shock therapy, the 500 c.e. is made up of 250 c.e. of ordinary pooled plasma and 250 c.e. of saline. In this instance there is no saline added, and the whole 500 c.e. is pure plasma. It is remarkable how quickly the edema lessens, the weight decreases, and the woman voids an appreciably increased amount of urine. None has required a second transfusion nor any further treatment, except a continuation of balance. Amigen is not used. It is, of course, ideal in that it includes all the amino acids necessary for growth and development, but amigen in its present state can be given only in solution, and requires 1,000 c.e. of fluid to administer its protein. We are afraid of fluid in these cases.

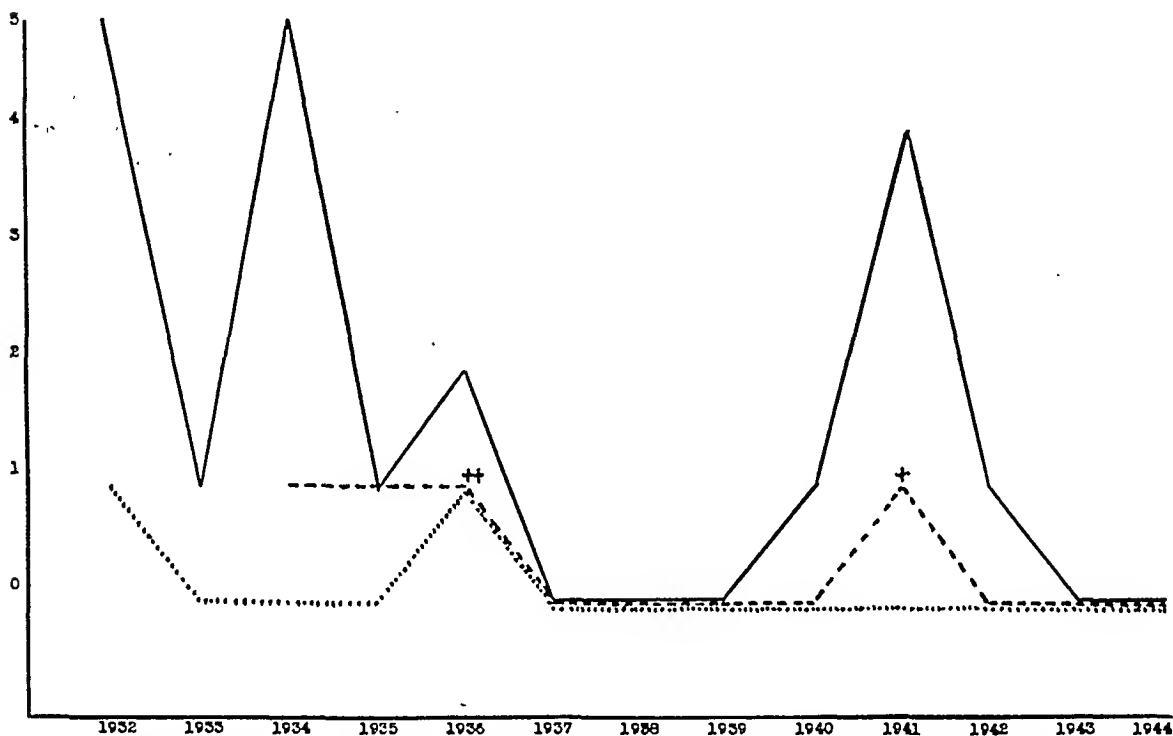


Fig. 1.—Incidence of eclampsia and eclamptic mortality.

— Total cases of eclampsia.

--- Patients treated antepartum by dehydration and fluid balance (begun June, 1934).

.... Deaths from eclampsia.

+ Postpartum eclampsia due to accidental discontinuance of treatment.

++ Doctor "became anxious." Discontinued treatment. Patient died.

## Results

It is interesting to note that in these 325 cases there were only two that reached the delivery stage and the delivery room with edema; one was a chronic nephritic, and the other a cardiac patient. There were in the whole group only 32 cases that showed even the slightest transient edema throughout the antenatal period. It might be well here to state that we believe the onset of "toxemia" is concerned with improper water metabolism. The general statistics of the hospital, as shown in the accompanying chart (Fig. 1), show conclusively the effect of this effort in the reduction of true, pure "toxemia." It shows also the total abolition of eclampsia since 1936, where this routine has been used. The only exception was a postpartum eclampsia in which



restriction was accidentally discontinued on delivery of the patient. There has not been a death from eclampsia since 1936, and only one since 1933 and, in this instance the treatment was not used. Likewise, there were in this group of 325, 27 cases that exhibited a transient blood pressure rise of 20 mm. or more, five of these being over 30 mm. and one over 40 mm., but none of these reached the hospital with anything but a normal reading. These transient rises would be ordinarily disregarded, but they were the nearest approach to pre-eclampsia that was observed. The absence of albuminuria was remarkable. In these cases we were able to find only nine specimens that showed an appreciable amount of albumin.

But there were other advantages: the remarkably low incidence of abnormal presentation; the abnormally low incidence of primary cesarean section for bony and soft tissue dystocia; the stillbirth record; and the marked diminution in length of labor. Taking them in order: posterior positions occurred, but did not cause the dystocia that we would expect in the type of patient that was handled. There were only twelve forceps rotations in primiparas, and two in multiparas; eleven mid-forceps, all in primiparas; there were no versions, except for a second twin. There were six breech presentations each for multiparas and primiparas. There was only one cesarean section for dystocia. There was a total of eleven cesarean sections. Four were in primiparas: the first for very severe rheumatic heart disease, the second for a mole with a term child causing profuse hemorrhage, the third for placenta previa centralis, and the fourth for dystocia. There were no primary sections in multiparas, but there were seven repeat sections in this group. This gave us an incidence of primary cesarean section of 1 in 81.2, and a rate of 1.2 per cent; and an incidence of cesarean section for dystocia of 1 in 325, or .003 per cent. This relatively low rate of abnormal delivery was in keeping with the ease with which these patients had their babies. Practically all of these patients were delivered by low forceps or outlet forceps. For example, only 16 primiparas spontaneously delivered, mostly because I did not have time to do anything else, and 94 multiparas delivered spontaneously for the same reason. One hundred seven primiparas and 59 multiparas were delivered by low or outlet forceps. There were five stillbirths, a rate of 1.53 per cent. This compares very favorably with the stillbirth rate of the Chicago Lying-in Hospital,<sup>1</sup> which was reported as 2.14 per cent, and that reported by Kernis<sup>1</sup> of 5.2 per cent, and that reported by Sloan<sup>1</sup> of 4.4 per cent; but of course, these were in a larger series of cases. These five stillbirths were not attributable to delivery. One was a mole with a living child that died just before cesarean section; one was a macerated twin; the third was another macerated child at term with the cord tightly twisted about its neck; the fourth was an anencephalic monster; and the fifth was a fetus with polycystic kidneys. There were no fetal deaths from prolonged or difficult labor. There were two neonatal deaths: two prematures; one following a cesarean section for central placenta previa, and one following an abruptio placenta with massive external hemorrhage treated conservatively.

It is important to note that the average age of these patients is higher than normal, being 29.4 years, and the problems arising from just the fact of the age have been minimized, it is believed, by this routine.

The effect of this routine on the length of labor and the other factors that are problems in the ordinary labor cases may now be considered. The average age of these patients was 29.41 years. The 159 primiparas averaged 27.47 years, and the 166 multiparas 31.36 years. This was definitely not a young group. There were, for example, 53 primiparas and 114 multiparas over 30 years of age. That is exactly one-third of the primiparas, and exactly two-thirds of the

multiparas over 30 years, and 51 per cent of the whole 325 over 30 years. The younger patients were the hardest to handle because of previous lack of care. Many of them had reached "blimp" proportions when we saw them. The overall gain of all patients was only 14.9 pounds, the primiparas averaging 15.4 and the multiparas averaging 14.3 pounds. The average labor of the group was 6 hours and 17 minutes, primiparas being 7.19 and the multiparas 5.15 hours. This short duration of labor was obtained in spite of six cases of cervical dystocia and eight cases of uterine inertia. Presented again, the average weight gain for 325 cases was only 14.9 pounds, the average age was 29.4 years, and yet the average length of labor was only 6 hours and 17 minutes. This was consistent with the facts of the first paragraph, namely, that it is possible to have shortened labors as a result of satisfactory food control, diet, and fluid balance, and exercise.

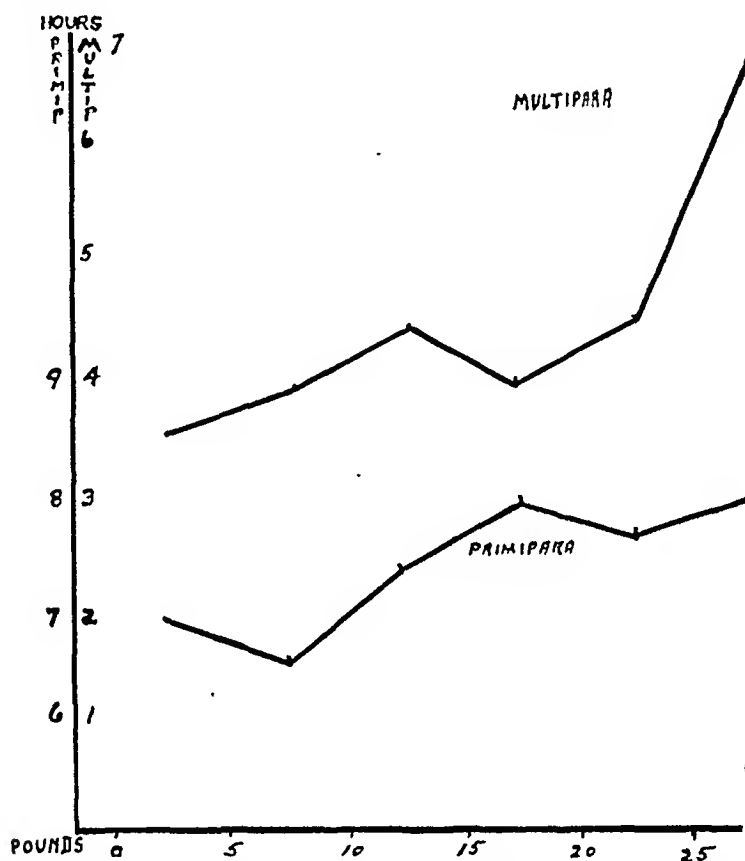


Fig. 2.—Effect of weight gain, diet, and fluid balance on length of labor.

The babies in this series were all average in size. There was no baby that was abnormally small and there were none extremely large, but, in many instances, the largest babies were born to mothers who made no gain or a minimal gain. In one instance, a very stout woman who gained no weight delivered a 9-pound baby, and, from these records, we can only corroborate the work of previous investigators who have shown conclusively that there is no reduction generally in the weight of the baby due to restriction in diet. It is true, of course, that there were no extremely heavy babies, but there were some solid, large children. There were no fetal deaths from dystocia. There was no toxemia and no difficult deliveries, except in three cases of cervical dystocia which were delivered under caudal anesthesia. Yet, to accomplish this, all that seems to be necessary is to use some self-evident facts, faithfully and diligently, some outmoded exercises, and, unfortunately for the obstetrician, a great amount of tough perserverance.

In Fig. 2, the relationship between weight gain and length of labor is graphically presented. There is a definite lengthening of labor as the weight increases, but the labors were all fairly short.

In Fig. 3, the effect of weight gain on dystocia is shown. The higher rate in the 0- to 5-pound group, and in the 5- to 10-pound group was expected by the difficult type of case in these groups. The dotted line shows only a trend, as the cases were too few.

In Fig. 4, the effect of weight gain on an arbitrary standard of toxemia is demonstrated. The curve is the same as in Figs. 2 and 3, and is presented for what it is worth.

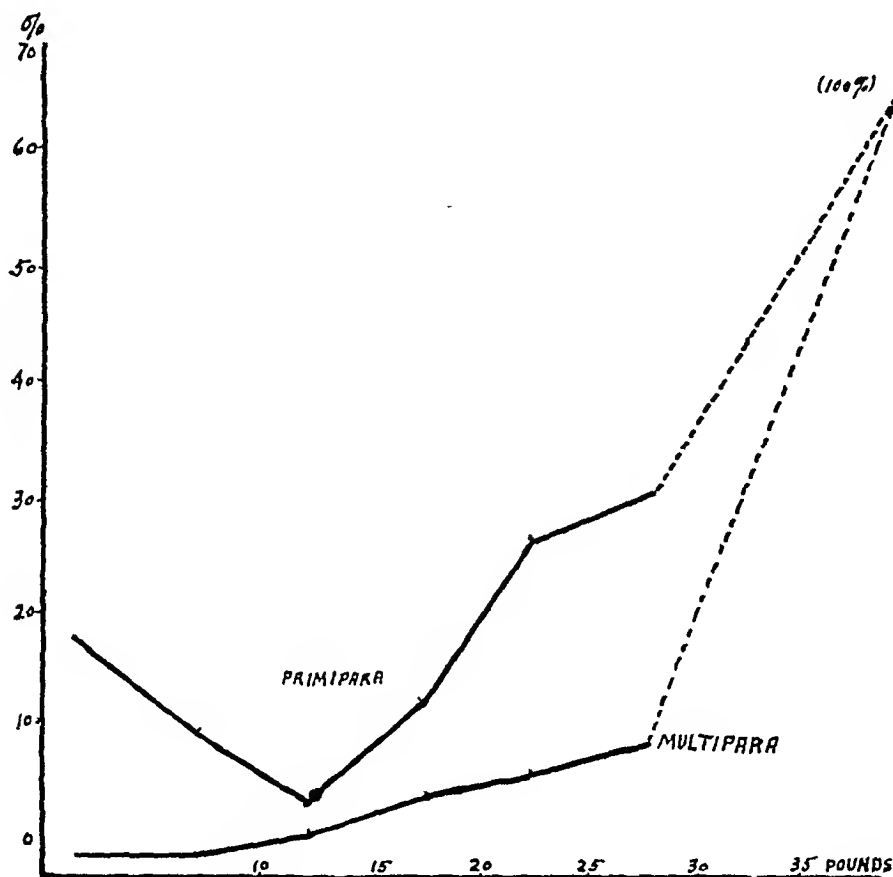


Fig. 3.—Effect of weight gain, diet, and fluid balance on dystocia.

For further observation, in more detail, the gains have been divided into groups for convenience. They are of approximately 5 pounds each. The first chart, Table I, shows the grains from 0 to 4 pounds, plus the cases which lost weight. As a matter of fact, one patient lost 32 pounds. This group is the difficult group. The primiparas here averaged over 28 years of age, 16 of the 19 being over 25 years, and 13 of them over 26 years. They were the obese patients, the ones with abnormal pelvises, the ones with whom we ordinarily would expect trouble. It includes some cardiacs, one a very bad cardiac; and as a result of the regimen, the average labor was only 6.9 hours, and the weight was kept to 1.7 pounds average (the 32-pound loss in a bad cardiac was not included). In spite of this, the incidence of abnormalities was fairly high, but when we consider the type of case that was handled in this group, the results, I feel, were good. The only primary cesarean section for dystocia in the whole group occurred here. It was necessary, for the patient was a 26-year-old, very

obese, pituitary type woman, having a cephalopelvic disproportion due to a very definite android pelvis. She was sectioned after a six-hour test of labor. Peculiarly, the four primary cesareans, as previously described, occurred here. None of the other three were due to dystocia, as previously noted. There were three midforeeps rotations, and only one patient showed any transient edema. The multiparas fared even better, with a 29-year average and an average gain of 3.35 pounds. The average length of labor for this group, all of whom were over 25 years of age, was 3.8 hours; none developed even a transient edema; and there was not one abnormal delivery.

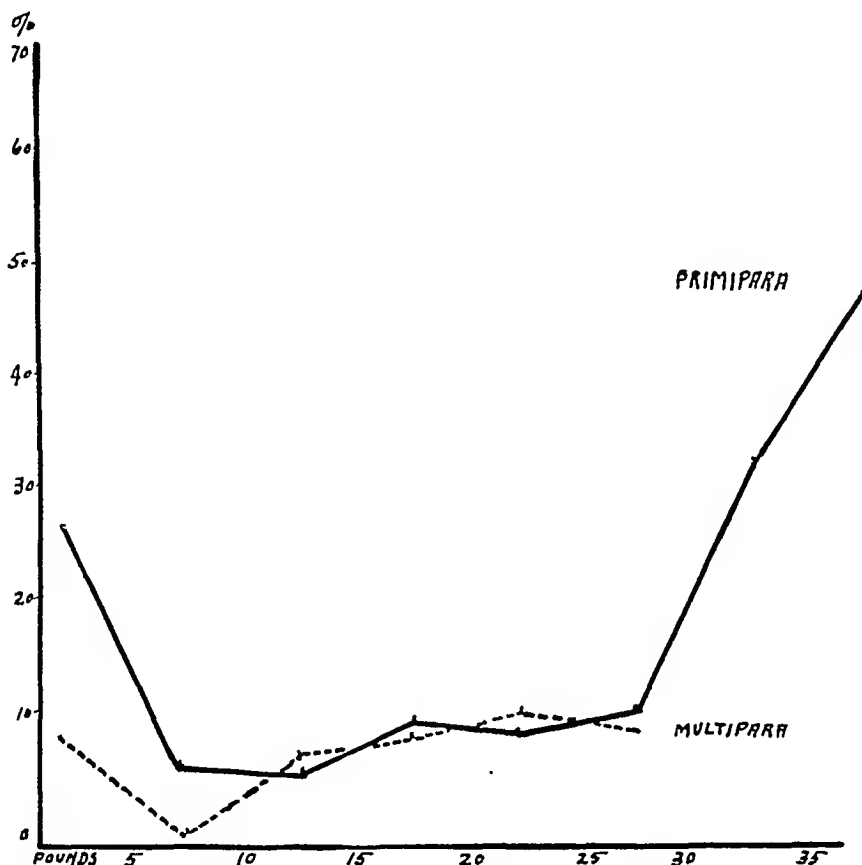


Fig. 4.—Effect of weight gain, diet, and fluid balance on blood pressure. Transient rise of 20 mm. or more.

Considering the second group who gained 5 to 9 pounds, there were 38 patients. These, too, contained the difficult type of case that we are anxious to control thoroughly. This primiparous group was also over 28 years, had an average gain of 8 pounds, and yet had a labor rate of only 6.6 hours. There was only one midforeeps delivery in this group, none of them showed any evidence of a toxie state except two that presented a very transient edema, and one that showed a temporary rise of 20 mm. in blood pressure. The multiparas did even better, showing no complications whatsoever. The group gaining 10 to 14 pounds numbered 93 (Table I); the primiparas were well over 29 years' average, showing an average gain of 12.6 pounds and an average labor of 7.4 hours. There was only one midforeeps delivery in this group and two foreeps rotations, but we began to show a slight increase in tendency to complications because both the multiparas and primiparas together included six cases with a temporary blood pressure rise of over 20 mm.

In the 15- to 19-pound gain group we had 87 patients (Table I). The age is a little lower, 26.3 years for the primiparas and 30.68 for the multiparas.

TABLE I. TABULATION OF CASES IN GROUPS

PRIMIPARA		MULTIPARA
<i>Group Gaining Less Than 1 to 4 lbs. (31 cases)</i>		
19	Total number	12
28.6	Average age	29.66
1.67	Average weight gain	3.35
6.9	Average length of labor	3.8
1. A difficult group: includes the very obese, the pituitary cases, obvious obstetric difficulties, and some cardiovascular diseases. 2. Results were good. Dystocia evidenced by only three midforceps rotations and 1 cesarean section. 3. However, all primary sections occurred in this group. 4. No evidence of severe toxic state. One in each group showed a transient blood pressure rise of 20 mm.		
<i>Group Gaining 5 to 9 lbs. (38 cases)</i>		
17	Total number	21
28.2	Average age	33.3
8	Average weight gain	8.13
6.6	Average length of labor	3.98
<i>Results</i>		
0	Cesareans	1 (repeat)
1	Midforceps	0
2	Transient edema	0
0	Blood pressure (trans. rise of 20 mm.)	0
<i>Group Gaining 10 to 14 lbs. (93 cases)</i>		
37	Total number	56
29.7	Average age	32.0
12.6	Average weight gain	12.32
7.4	Average length of labor	4.38
<i>Results</i>		
0	Cesareans	2 (repeat)
1	Midforceps	0
2	Forceps rotation	1
2	Total blood pressure rise 20 mm. plus	4
<i>Group Gaining 15 to 19 lbs. (87 cases)</i>		
39	Total number	48
26.3	Average age	30.68
17.4	Average weight gain	17.06
7.94	Average length of labor	4.05
<i>Results</i>		
0	Cesareans	3 (repeat)
1	Midforceps	1
2	Midforceps rotation	0
4	Transient edema	2
4	Transient blood pressure rise 20 mm. plus	4
<i>Group Gaining 20 to 24 lbs. (48 cases)</i>		
31	Total number	17
25.93	Average age	30.11
22.47	Average weight gain	21.73
7.77	Average length of labor	4.37
<i>Results</i>		
0	Cesareans	1 (repeat)
4	Forceps rotation	0
2	Midforceps	0
5	Transient edema	1
3	Transient blood pressure rise 20 mm. plus	2

PRIMIPARA		MULTIPARA
<i>Group gaining 25 to 29 lbs. (19 cases)</i>		
9	Total number	10
25.66	Average age	29.5
26.47	Average weight gain	25.82
8	Average length of labor	7.13 plus
<i>Results</i>		
0	Cesareans	0
2	Midforceps	1
0	Forceps rotation	0
3	Transient edema	2
1	Transient blood pressure rise 20 mm. plus	1
<i>Group Gaining 35 to 39 lbs. (5 cases)</i>		
21.5	Average age	26
35.87	Average weight gain	35.25
7	Average length of labor	8.5
All cases became difficult.		
All met some dystocia.		
All required dehydration.		
All had temporary severe blood pressure rises.		
All primiparas were under 26 years of age.		

Their average weight gain was 17.4 pounds in primiparas and 17.06 pounds in multiparas, respectively, and their labor was a little longer, averaging 7.94 and 4.05 hours. Here we met a slight and definite increase in complications. In this group there were three midforceps rotations, six that showed a transient edema, and eight that had a temporary rise of blood pressure over 20 mm. We have had to take this low standard because it was the only point at which we could attempt to evaluate the blood pressure changes. It is realized, of course, that a 20 or 30 mm. change in blood pressure transiently is not regarded as of any particular importance, but as there was not any great change in any of these patients, it has been used as a standard for what it is worth.

In the succeeding group showing a (Table I) 20- to 24-pound gain, the number decreases to 48. The average age for primiparas decreases to 25.93 years, and their weight gain is 22.47 pounds. The multiparas gained 21.73 pounds, and the length of labor is about the same as the previous group, 7.77 and 4.37 hours. We notice in our evaluation of this group that four of these primiparas required forceps rotation; two, midforceps delivery; five showed a very transient edema; and three of them a blood pressure rise of 20 mm. or more. The multiparas did better in an absence of dystocia, but their tendency to toxic state was proportionately even worse. The percentage in Table II is much higher than in the previous group.

The 25- to 29-pound gain group is reduced to a total of 19, so that I have not been able to include fairly these in the graphs, but, nevertheless, the labor in what we did have was very markedly lengthened and the complications proportionately increased.

The last group, totalling only four, is hardly a fair estimate of what occurs, but it is significant that this group with an average gain for the primiparas of 35.87 pounds and the multiparas of 35.25 pounds were the most difficult. Every one of them had a very definite blood pressure rise and some obstetric and dystocia difficulty. It is also peculiar that in the last two groups, totalling eight patients all were under 26 years of age. Evidently, their relatively short labors of 7 hours and 8.5 hours, respectively, were somewhat assisted by their youth.

TABLE II. RECAPITULATION

WEIGHT GAINS BY GROUPS (POUNDS)		TOTAL NUMBER	LENGTH OF LABOR (HOURS)	DYSTOCIA	BLOOD PRESSURE VARIATION 20 MM. OR OVER
0-4	P	19	6.9	4 or 21%	1 or 20.8%
	M	12	3.8	0 or 0%	1 or 8.3%
5-9	P	17	6.6	2 or 11.7%	1 or 5.8%
	M	21	3.98	0 or 0%	
10-14	P	37	7.4	2 or 5.4%	2 or 5.4%
	M	56	4.38	1 or 1.7%	4 or 7.1%
15-19	P	39	7.94	5 or 12.8%	4 or 10.2%
	M	48	4.05	2 or 4.1%	4 or 8.3%
20-24	P	31	7.77	9 or 29.2%	3 or 9.6%
	M	17	4.37	1 or 5.8%	2 or 11.7%
25-29	P	9	8.00	3 or 33.3%	1 or 11.1%
	M	10	7.13	1 or 10%	1 or 10%
30-34	P	3	5.91	0	1 or 33.3%
	M	1	5.00	0	-
35-39	P	4	7.1	4 or 100%	2 or 50%
	M	1	8.5	1 or 100%	-

### Summary and Conclusions

From these figures, of course, we can draw no definite conclusions, we can just infer with a definite question mark as to what exactly is the controlling factor and why it is that these labors were so short. When we realize that the average labor as given by DeLee<sup>1</sup> is 18 hours for primiparas, 12½ for multiparas, and 27 hours for elderly primiparas, and by Beck<sup>7</sup> as 18 hours for primiparas and 12 hours for multiparas, and yet ours are so much shorter, we begin to wonder if the regimen as described is not responsible for this happy situation. This means definite lessening of pain; less sedation than in the prolonged labor; less trauma to the baby; less supportive treatment; and less effort for the obstetrician and hospital personnel. In many of these patients, the progress is so rapid that sedation is not possible, except nitrous-oxide in the latter part of the second stage. Delivery in these cases was in no way forced. These accouchments were all handled conservatively, the only "radical" thing being outlet forceps and episiotomy. No patient was allowed to stay in labor unduly long, but no case was delivered before the proper time. All cases were delivered under gas-oxygen or gas-oxygen-ether anesthesia, except the cervical dystocias which were given a single injection caudal or low spinal anesthetic and delivery completed in each instance with ease. The fact of lessened analgesia gives us a very satisfying incidence of asphyxia neonatorum.

These statistics, under this plan of prenatal care, are presented merely as an interesting observation. We realize, of course, that many men do use many parts of this treatment for the established "toxie," but there are many others who totally ignore what we consider the earliest evidences of toxemia, namely, fluid retention. It is strongly felt that continued marked retention invites disaster, and neglect of the factors here under discussion invite obstetric difficulties that require time and worry and difficult procedures to overcome.

We have presented 325 cases in which, in conjunction with a regimen previously described, the length of labor has been markedly decreased; the incidence of dystocia markedly lessened; and any real toxic state totally absent, except in one case of chronic nephritis which we do not believe is in any way influenced by this type of regimen. This case was induced and is the only induction in the series. Three severe cases of hypertensive cardiovascular disease were decidedly improved and were uneventfully delivered. It is believed that these results can be reproduced at will in the patient who is willing to cooperate, if a high protein, high vitamin, and low carbohydrate diet is instituted, a very definite amount of exercise is included, and the fluid balance is properly maintained. There was no mortality.

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277 PARK PLACE



## THERAPEUTIC ABORTION IN A GENERAL HOSPITAL\*

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DURING the past few years, I have been called upon to assist officers of the Drug Division of the United States Food and Drug Administration in the preparation of evidence for the institution of legal action against the manufacturers and distributors of abortifacient pastes.<sup>1</sup> It was essential to supply testimony which would emphasize the many dangers involved in the use of such pastes, and which would refute the various claims made on the printed labels. In one instance, it was necessary to offer statistical data to controvert the statement that therapeutic abortions are frequently indicated, therefore all cases on which a therapeutic abortion had been done at the New York Post-Graduate Hospital during a ten-year period were reviewed (Table I).

TABLE I. THERAPEUTIC ABORTIONS DURING A TEN-YEAR PERIOD AT THE NEW YORK POST-GRADUATE HOSPITAL

By the Director of the Gynecological Service	34
By other gynecologists	39
By general surgeons	11
Total	84

It is perhaps natural that the majority of patients should gravitate to the Director of the Gynecological Service, who performed about 40 per cent of the abortions done. Before the publication of a recent paper by Cosgrove and Carter,<sup>2</sup> in which only four interruptions of pregnancies were reported in 67,000 deliveries at the Margaret Hague Maternity Hospital, the number of our cases, 84, and the incidence of our therapeutic abortions seemed creditably low. Both the extremely small number of induced abortions and the astonishingly few indications for the termination of pregnancies in the Margaret Hague Maternity came as a surprise to one who has conscientiously tried to regulate therapeutic abortions under his control to those conditions for which they are regarded as justified for the protection and prolongation of the mother's life. In one of Cosgrove's and Carter's cases, abortion was done for hyperemesis gravidarum, and three others were for hypertension and nephritis. Realizing that the Margaret Hague Maternity is but an obstetric unit adjoining the Jersey City Medical Center, it might be assumed that the largest percentage of therapeutic abortions were performed in either the gynecologic or general surgical departments, or both, but in a personal communication Doctor Cosgrove stated that this was not so. Despite making generous allowances for ultraconservatism, the discrepancy between the statistics of a strictly maternity hospital and a general

\*Read before the New York Obstetrical Society, Nov. 13, 1945.

hospital is so startling that it seemed desirable to scrutinize in some detail the same 84 cases at the New York Post-Graduate Hospital which I had utilized previously for expert testimony in the Federal Court.

In selecting the material from which to compile this statistical evidence, all pediatric, orthopedic, dermatologic, and male patients were excluded, thus limiting the basis for the figures used to adult females (Table II).

It is apparent that, of the 84 induced abortions, 55, or more than one-half, were ward cases, which indicates that most of them were done on patients of low income levels.

TABLE II

Gynecologic and female surgical hospital admissions		29,516
Therapeutic abortions	84	
New female adult admissions to all clinics exclusive of the Dermatological Clinic		172,552
Therapeutic abortions—ward cases	55	

TABLE III

Gynecologic admissions to hospital		4,871
Therapeutic abortions by the Director of Service	34	
Therapeutic abortions by other gynecologists	39	
Total	73	
Per cent of therapeutic abortions in gynecologic hospital admissions (including 18 private patients)		1.49
Surgical admissions to hospital (female)		24,645
Therapeutic abortions by general surgeons (all private patients)	11	
Per cent of therapeutic abortions done on the surgical service by general surgeons		0.04
Per cent of therapeutic abortions in 25,516 adult female hospital admissions		0.28

Table III shows that 11 abortions were done by general surgeons and 18 by gynecologists, a total of 29, on semiprivate and private room patients. However, a hospital rule pertaining to therapeutic abortions has been in effect for the past few years, which applies to all patients, regardless of their hospital status, and every operator, and reads as follows: "In cases of therapeutic abortions the indications must be indorsed in writing by two members of the Attending Staff of the New York Post-Graduate Hospital; one shall be the operating surgeon, and one a physician specializing in the condition necessitating the procedure, or a recognized specialist whose qualifications are acceptable to the Superintendent of the Hospital." It must be admitted that, while the majority of these therapeutic abortions were done to preserve the mother's health, to prolong her life, and to prevent serious and permanent injury, under the direction of at least two licensed practitioners of medicine the life of the mother was not always threatened imminently.

The inherent risk to the mother involved in a surgically clean and thorough therapeutic abortion, performed by a capable pelvic surgeon in a modern hospital operating room, barring surgical accidents, is *nil*. Seventy-four of our patients were operated on between the third and twelfth weeks of pregnancy, and the other ten between the thirteenth and eighteenth weeks. The average operating time was sixteen minutes, and there was no maternal mortality in

the 84 cases. If it is the duty of the profession to save and conserve human life, and if as the old English common law holds, the unborn child, prior to quickening, has no entity, then the physician's conscience and judgment must dictate which is entitled to greater consideration: the future life and health of the mother or the possible future life of a still nonviable fetus. It may be conceded that the nonviable fetus is entitled to the protection of its life potentialities in normal cases, but when such conservatism seriously jeopardizes the life and health of an already living human being, it is not unnatural that the laws of most States should recognize that licensed physicians must accept certain responsibilities, and establish their own ethical standards on a strictly medical basis. On the other hand, social problems and economic considerations should never influence a decision to the slightest degree.

There is a great difference between the removal of all deterrents to the practice of therapeutic abortions and the interruption of pregnancy for serious physical ailments under proper, honest, and strictly controlled medical supervision. I would question the implication that a conscientious and well-qualified obstetrician or gynecologist should be stigmatized as a mere mechanic to carry out the advice of a specialist in another field, just because he may rely to a certain extent on the latter's experience and opinion. The decision in each individual case should rest upon the combined judgment of at least two physicians of wide experience, but it is not unnatural that the opinion of the one who is really expert in the treatment of the particular condition that constitutes the reason for the interference should carry considerable weight. The indications for the termination of pregnancy in our 84 cases are classified in Table IV.

TABLE IV. INDICATIONS FOR THERAPEUTIC ABORTION

Cardiovascular disease	20
Psychoneurological diseases	14
Renal disease	12
Hyperthyroidism	9
Tuberculosis	8
Persistent hyperemesis gravidarum	3
Miscellaneous	18
Total	84

All of our patients were white women, the youngest being 19 years and the oldest 43 years of age. Thirteen patients had had one or more previous therapeutic abortions. Eight patients had additional surgical procedures done simultaneously with the curettage or vaginal hysterotomy. In only 15 instances was the abortion done for the patient's first pregnancy, the other 69 all being multigravidas.

*Cardiovascular Disease.*—In fifteen of the twenty cases in which cardiovascular disease was the indication for therapeutic abortion (Table V), mitral stenosis with insufficiency was the predominating feature, and all were classified as 2B or more severe by the cardiologist. One of these patients had a history of several previous episodes of decompensation, two had a concomitant aortic insufficiency with marked hypertrophy, one had coexisting multiple fibroids, and another a large ovarian cyst. Two patients had serious hypertensive cardiovascular disease, and one of them developed a progressive hyperemesis gravid-

TABLE V

Mitral stenosis	15
Hypertensive cardiovascular disease	2
Congenital heart disease	1
Heart disease with multiple complications	1
Unclassified	1
Total	20

arum, which failed to improve under appropriate therapy. One patient with congenital heart disease was classified as 2B, and another had marked cardiac arrhythmia with premature ventricular contractions, thyroid dysfunction, cholecystitis, and secondary anemia. The details on the chart of one patient, aborted by a senior member of the attending staff, now deceased and whose private records are not available for review, are incomplete, so that this case cannot be correctly evaluated. Ten of the twenty patients originated in the cardiac clinic, where all patients are seen by not one cardiologist, but several.

TABLE VI. PSYCHONEUROLOGICAL DISEASE

Dementia precox	3
Maniac depressive psychosis	3
Epilepsy	4
Neurosyphilis	2
Malignant brain tumor	1
Muscular dystrophy	1
Total	14

*Psychoneurological Diseases.*—The six cases of mental disease and the four epileptics (Table VI) had been diagnosed as such long before the interruption of pregnancy, and all fourteen patients were referred to the gynecologic service by a senior attending psychiatrist, neurologist, or neurosurgeon. One patient with neurosyphilis had bilateral optic atrophy and complete blindness. Another after two years of treatment, was still Wassermann fast and showed signs of mental deterioration. The patient with the malignant brain tumor had also had a previous resection of the eighth cranial nerve.

TABLE VII. RENAL DISEASE

Chronic glomerular nephritis	6
Solitary kidney	3
Nephrolithiasis	2
Pyelonephritis	1
Total	12

*Renal Disease.*—The six cases of glomerular nephritis (Table VII) were all proved by laboratory tests and were seen by consulting internists and urologists. One had an associated aortic stenosis, another had an independent hypertensive cardiovascular disease, and another had had four previous toxemias of pregnancy. One patient with a solitary kidney had the other one removed three years previously for renal tuberculosis, and when referred for the abortion still had active pulmonary tuberculosis and a tuberculous colitis. Another, aged 31 years, who had one living child, had had a nephrectomy for a large hydronephrosis two years previously, and suddenly developed acute urinary obstruction from a ureteral stricture on the other side. The third, aged 34 years, who had three living children, had a nephrectomy for a contracted infected kidney

secondary to nephrolithiasis, and the remaining kidney showed evidence of marked chronic nephritis, as indicated by the blood chemistry, urine, and renal function tests. One patient with nephrolithiasis was transferred four days after the abortion to the urological service for pyelotomy. The other one had bilateral renal stones with pyonephrosis. The patient with bilateral pyelonephritis was 37 years old, a para ii, and became progressively worse instead of better despite prolonged treatment in the urological clinic.

*Tuberculosis.*—All eight patients, aborted because of tuberculous, had active and far-advanced pulmonary tuberculosis, proved by x-ray examination, and five of them had grave complications (Table VIII).

TABLE VIII. TUBERCULOSIS

Advanced pulmonary tuberculosis	3
with tuberculous rhinitis, bursitis, and urogenital tuberculosis	1
with empyema	1
with pneumothorax	1
with previous thoracoplasty	1
with duodenal ulcer and cholecystitis	1
Total	8

*Thyroid Disease.*—Therapeutic abortion was indicated in nine cases of thyroid disease. The patients classified as having severe hyperthyroidism had basal metabolic rates of plus 42, 32, and 24, respectively, and the second one had coexisting hypertensive cardiovascular disease, with a blood pressure of 190/112. One of the five patients with persistent hyperthyroidism after thyroidectomy had been operated upon twice before, and when she entered the hospital for a third thyroidectomy was found to be pregnant. The patient with carcinoma of the thyroid had had a thyroidectomy two years previously, which was followed one year later by a radical neck dissection for recurrent carcinoma in the cervical lymph nodes.

TABLE IX. THYROID DISEASE

Severe hyperthyroidism	3
Persistent hyperthyroidism after previous thyroidectomy	5
Carcinoma	1
Total	9

TABLE X

Persistent hyperemesis gravidarum	3
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Two patients were aborted for uncontrollable hyperemesis gravidarum, but one had to be aborted a second time within two years (Table X). She was a gravida ii, with a history of a severe toxemia of pregnancy before a delivery two years before, and was treated in the hospital for thirteen days, when she improved enough to be discharged. One week later she was readmitted with severe vomiting, a rise in blood nitrogen and uric acid, plus 3 acetone, plus 2 diacetic acid, and albuminuria, and was aborted after twelve days of ineffectual treatment. One year later the uterus was emptied again for the same reasons. The second patient, a gravida i, para i, had had a difficult labor, and entered the hospital with a severe hyperemesis, which became progressively worse after five days of treatment, complicated by a maniac depressive psychosis and suicidal tendencies.

TABLE XI. MISCELLANEOUS

Banti's disease with splenectomy	1
Maternal blood dyscrasia with three previous abnormal babies	1
Impetigo herpetiformis	1
Acute rheumatoid arthritis	1
Severe uncontrollable diabetes	2
Chronic interstitial hepatitis	1
Severe constitutional and metabolic impairment	1
Postpartum psychosis after previous cesarean section for contracted pelvis	1
Surgical complications	
Previous plastic repairs	2
Pelvic peritonitis and ovarian cyst	2
Rectovaginal fistula and hyperthyroidism	1
Therapeutic errors	
Malignancy of uterus	1
Previous placenta previa	1
Phlebitis	1
Lumbosacral pathology	1
Total	18

The patient with Banti's disease had a splenectomy and biopsy from the liver four years previously. She had recurring leucocytosis, fever, and gastric hemorrhages.

A gravida iii, suffering from a recurring secondary anemia, had been delivered by the same physician of three babies, all of whom were apparently born with erythroblastosis, before the importance of the Rh blood factor was appreciated by obstetricians. The last one also had a marked jaundice and only 27 per cent hemoglobin, requiring three transfusions. Despite liver and iron therapy the patient was still very anemic and was aborted at the seventh week after she became pregnant again.

The patient with impetigo herpetiformis was referred by Doctor George Miller Mac Kee, after having been seen by all the senior dermatologists at the Post-Graduate Hospital. Doctor Mac Kee is my authority for the statement that impetigo herpetiformis is an extremely rare disease of mysterious origin, occurring only in pregnant women. Not more than twenty-five cases have been reported in the literature, and only three of them were in this country. The only known treatment of any avail is prompt abortion, and, notwithstanding the interference, about 85 per cent of the patients die. Our patient improved enough to leave the hospital six months after the abortion, but died of the disease about a year later.

The patient with acute rheumatoid arthritis was showing progressive advancement of the disease with erosions of the bones and a very high blood sedimentation rate, and was under treatment with gold salts.

Both diabetic patients had been under treatment for several years, and in both instances it was impossible to get the urine sugar or acetone free. The first one was 41 years of age and had three living children. The second had eclampsia with a delivery five years previously, and two weeks later had to have a laparotomy, which was followed by acidosis and coma, with a blood carbon dioxide combining power of 27. All blood sugar readings for five years had been over 200. At the time of her admission for therapeutic abortion the urine showed sugar 4 plus, acetone 3 plus, and diacetic acid 2 plus, and the blood carbon dioxide combining power was 35.

The patient with hepatitis had four pregnancies in the previous five years. She had had a recent cholecystectomy and was seen in consultation with both a surgeon and an internist.

A patient in a serious physical condition, with anemia and severe constitutional and metabolic impairment, who had had three previous pregnancies, was aborted after consultation with an internist and another gynecologist.

A 37-year-old gravida ii, who developed a severe anemia with each pregnancy, both of which were terminated by cesarean section for contracted pelvis, developed a postpartum psychosis after the last one, and became pregnant again before it cleared up.

Two patients were aborted because of extensive plastic repairs. The first one was a gravida iii, who had developed a rectovaginal fistula above a complete perineal laceration. Two previous attempts at repair had been made elsewhere before I operated on her successfully. Two years later she was aborted. The other woman was 40 years old, a gravida ii, and had also had an extensive plastic repair for a complete laceration, with amputation of the cervix. It is true that both of these patients might have been allowed to go to term and be delivered by cesarean section, but they both had living children, and it seemed unwise to risk another breakdown incidental to the circulatory changes during the last weeks of pregnancy.

Two patients were aborted incidentally during operations for extensive pelvic agglutinations and large ovarian cysts. The first one had three children, and had had a previous laparotomy. The third delivery, eighteen months before, had been followed by acute pelvic peritonitis. Since then she had suffered from intense pelvic pain, which for the last two months had become almost unbearable. The abortion was done before a technically difficult laparotomy. The second patient was much like the first one, except that she had had two previous laparotomies, including some sort of uterine fixation. Evacuation of the products of conception was difficult, and her pelvic adhesions and ovarian cyst had caused an intestinal obstruction.

A patient with a fresh rectovaginal fistula and third degree perineal tear and hyperthyroidism was aborted at the time of the plastic repair, prior to her thyroidectomy.

There were four cases which may be charitably designated as therapeutic errors. They were all performed before the days when formal consultation was made mandatory. The first patient was 31 years of age, and a gravida iii. She had continuous bleeding after the birth of her last baby six months previously. From this history, one might assume that the uterus was subinvolved or harbored some shreds of placenta. However, one of the senior general surgeons sent the patient into the hospital with a diagnosis of malignancy of the uterus, although he posted her operation as "therapeutic abortion, curettage, and frozen section," so he must have suspected the presence of the existing pregnancy. The pathologic report on the "curettage" showed a "fetus of the male sex and placenta." The logic, ideas, and procedures involved in this case are beyond my comprehension.

In a second case, also done by a general surgeon, the indication for the abortion was given as "prophylaxis as a health procedure because of nervousness, after a severe toxemia and placenta previa with her first pregnancy."

In a third case, also done by a general surgeon, the only indication seemed to be a long-standing phlebitis of the leg with swelling, cyanosis, and varicose veins.

In a fourth case, an abortion was done by a member of the gynecologic staff on the recommendation of an orthopedist, because of lumbosacral bone pathology. He should have known better.

Occasional professional lapses as exemplified by the records of these last four cases are no longer possible, and have not been for some time. Even before the adoption of the existing hospital rules pertaining to therapeutic abortions, practically all candidates for abortion were seen not only by one con-

sultant, but by several. The review of the charts utilized in the preparation of this paper has been quite enlightening, and although some errors on the side of liberality may have been made, I believe that most of the patients were treated correctly.

I am indebted to Doctor Henry P. Wager for his help in reviewing the case records and compiling much of the data therefrom.

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580 PARK AVENUE

### Discussion

DR. CHAS. GORDON HEYD (by invitation).—The occasions upon which a goiter surgeon seeks aid and counsel from the Gynecological Department for the purpose of inducing a therapeutic abortion are fortunately very few.

Continuing and persistent hyperthyroidism is a very disabling condition and occasionally lethal. The advent of pregnancy in an individual with hyperthyroidism adds to the basal metabolism of the mother the additional increment of the basal metabolism of the child. This additional basal metabolic rate of the child may be sufficient to induce an acute thyroid crisis with death. Therefore, there are two types of individuals with hyperthyroidism that warrant a consideration of the question of the artificial termination of pregnancy: (a) the patient already pregnant, with an hyperthyroidism; and (b) the postoperative hyperthyroid patient who becomes pregnant. In the first group we have come to certain definite conclusions. If the patient enters the hospital pregnant and with a well-defined hyperthyroidism we do not request an interruption of pregnancy, as a therapeutic abortion in a patient with a continuing and high hyperthyroidism may quite readily project that patient into an acute hyperthyroid crisis. After a short preoperative preparation we perform a subtotal thyroid resection irrespective of the pregnancy, for, with the amelioration of the hyperthyroidism by surgical intervention, the pregnancy may be allowed to continue to term. The risks inherent in thyroid surgery in a pregnant woman are no greater, if not less, than the dangers attendant on an interruption of her pregnancy. It is a rather interesting thing that spontaneous miscarriage following a thyroid resection in the pregnant woman is unusually rare and has occurred in our hands in only eleven consecutive cases.

In the second group, the postoperative thyroid patient who becomes pregnant, we have an entirely different problem. Here, we have a patient who has recently had a subtotal resection of the thyroid gland for hyperthyroidism. We believe that her future will be seriously endangered if she becomes pregnant within a year to eighteen months after her thyroid surgery, preferably not until two years have intervened between the thyroid surgery and her pregnancy. We are of the opinion that the continuation of pregnancy in this group carries with it a high incidence of recurrence of hyperthyroidism, one that is apt to be of more severe type than the original condition and inimical to the life and well-being of the mother.

Therefore, speaking for myself alone, I have no hesitation in asking for the termination of pregnancy in a young woman who has had a severe hyperthyroidism and who becomes pregnant after her thyroid surgery within a year to eighteen months. The delay, after the cure of such a condition, of eighteen months to two years before attempting pregnancy does not diminish their procreative potentialities, but it insures a healthy mother and a much healthier offspring.

DR. MORTIMER D. SPEISER.—I would like to ask Dr. Heyd whether he has had any experience with thiouracil in the group of patients with recurrent hyperthyroidism. It is my impression that with this drug some of these patients with recurrent hyperthyroidism might be carried to term.



DR. HEYD.—Dr. Speiser brought up an interesting question. Resection of the thyroid is the only means of permanently terminating hyperthyroidism. Thiouracil is capable of reducing a plus basal metabolism only as long as the patient takes the drug. It is, however, a dangerous drug, with 11 per cent toxic reaction and occasionally the cause of death by producing agranulocytosis. A pregnant woman with hyperthyroidism will not abort following resection of the thyroid. Accordingly, if the patient with hyperthyroidism is pregnant, we perform the thyroid surgery and let her continue her pregnancy. On the other hand, we urge the patient after a thyroid operation for hyperthyroidism not to become pregnant for a year to eighteen months on account of the liability of recurrent hyperthyroidism.

DR. CHARLES A. POINDEXTER (by invitation).—Patients with organic cardiovascular disease represent the largest groups in Dr. Dannreuther's series. Our Cardiac Clinic at the New York Post-Graduate Hospital is large. Quite naturally our census of rheumatic valvular disease is also large. To me these few cases seem to be quite small in number and represent an ultra-conservative attitude. We do not recommend abortion for cardiac patients unless we feel it is very necessary.

In diseases other than cardiovascular, socio-economic factors are not so important, but, before making a judgment, a cardiologist must look further than just the physical findings. He should know the conditions under which a patient must exist during the period of pregnancy. A social service report, particularly of home conditions and the potentiality for adequate care is necessary. The difference between excellent care at home as compared to climbing five or six flights of stairs several times a day and the burden of cooking and caring for several other children is tremendous. Socio-economic factors are important in heart disease and too often in statistical studies these factors are forgotten.

I would like to make a plea for a thorough cardiac study of each patient in order to evaluate the patient's cardiac status. It is a relatively simple matter to carry out such a study. This does not mean just an electrocardiogram and fluoroscopic examination. It means an extremely competent history in which an effort is made to actually evaluate what the patient is able to do physically, and attempt to evaluate the reaction of the heart to increased work such as pregnancy brings on. Of course, the examination usually includes electrocardiographic and fluoroscopic studies. It also includes, needless to say, a thorough general physical examination. But, of the necessary studies, probably the most important of all is to find out as best you can from the history exactly what the patient is able to do because, after all, that is the final test, and one cannot rely too much on the so-called functional tests which, in our experience, have been of little practical value.

Of the cardiac patients we have seen, most listed in Dr. Dannreuther's figures come under the classification of rheumatic heart disease with mitral stenosis. Mitral stenosis is a rather common heart lesion, particularly on the lower East Side, and it is a lesion which very often, most unfortunately, is not recognized. Therefore, I would like to remind you of a few simple diagnostic criteria, i.e., a presystolic or diastolic murmur, best heard at the apex of the heart. (This murmur is easily missed if you do not listen at the exact apex.) Another finding, frequently forgotten, is that patients with mitral stenosis do not have very much cardiac enlargement. It is only when trouble develops due to chronic failure mitral stenosis that heart enlargement occurs. In the average case no enlargement is discovered unless a careful fluoroscopic examination is made, and then the enlargement may be limited to the left auricle, and yet these are the patients who may get into trouble by having sudden failure.

There are one or two other factors that I would like to emphasize in connection with mitral stenosis, based upon our experience. When there is evidence of potential right heart failure, anything which will decrease the depth of respiration is likely to precipitate cardiac failure even in a patient who has been well compensated, and the patient may die very quickly. This is not seen as frequently in obstetrics as preoperatively. However, I believe it happens quite often in the second stage of labor during the time that the uterus is emptied during delivery. With the sudden decrease in intra-abdominal pressure, the return flow of blood to the right heart is diminished, and the vital capacity is decreased at the same time.

We do not know much about what pregnancy does to the future health and longevity of the cardiac patient. This problem is very difficult to evaluate and, with more experience, I am becoming more and more conservative about trying to say what pregnancy is going to do to the woman with heart disease. If one thinks he is going to get cardiac failure, the initial pregnancy is going to be a very important factor in shortening the patient's life. However, cardiac failure does not happen very often in pregnancy. In rheumatic heart disease, when failure does occur, I believe that pregnancy shortens the patient's life.

Statistical analyses dealing with morbidity and longevity are so technically difficult and fraught with so many variant errors, even with a seemingly adequate control group, that I believe we should be careful about personal observations made on a small series of cases.

In regard to the question of the 14 deaths in the group of 840 patients with rheumatic heart disease, as referred to by Dr. Norton, I would say that I do not know. Our cardiac cases are a somewhat selected group, culled for the purpose of teaching. We have, therefore, more of the advanced cases with severe valvular lesions. However, I do not think that 14 deaths are an exceedingly high number for a group of 840 cardiacs over a period of six years. Fourteen might die of the intercurrent failure anyway, but I think from our group of 1,200 patients, five therapeutic abortions would be far too small.

I don't see how anyone can divorce the socio-economic factors in the cardiac from this question of indications for abortion. I feel that it cannot honestly be done; it is too important a factor to ignore.

DR. EDWARD A. SCHUMANN (by invitation).—I was impressed in observing Dr. Dannreuther's statistics, when contrasting them with the statistics from the Margaret Hague Maternity Hospital, with the fact that these patients were admitted, not to an obstetrical institution, but to a general hospital. Therefore, they were viewed more from the standpoint of the coincident disease, such as hyperthyroidism and cardiac disease, as discussed by Dr. Poindexter, than the pregnancy itself. I make no doubt at all, with due respect to the essayist, that a number of these patients could have been carried through their pregnancy without undue disturbance rather than having abortions produced upon them, had they been originally admitted to a hospital such as Dr. Cosgrove's, where every emphasis is placed on the retention of pregnancy rather than the mere coincident disease. Consequently I feel that a number of them would not have been aborted and probably would have lived through it.

However, I am more and more impressed with the fact, and if you will pardon me, religious considerations aside, that we have been a little too much concerned with, let me say, the sanctity of pregnancy. Personally, in a member of my own family, if there was any consideration of disability or death from cardiac disease or hyperthyroidism or other indications, I would largely disregard an incipient pregnancy and have a small inconsequential fetus removed without concern to myself or to my patient. I think we are apt to be too hyperconservative and think too greatly about the fetus. At any rate, in this series of interrupted pregnancies, 84 in 25,000 hospital admissions (many of them were not concerned with pregnancy at all and another group was beyond the child-bearing age). Nevertheless, I still feel that in a large number of admissions, 84 terminations of pregnancy are not to be considered at all, and I wish to express myself as being in entire accord with the Post-Graduate Hospital in the termination of pregnancy with the greatest freedom if there is any danger to the life of the patient from the retention of that pregnancy.

DR. ROBERT A. MAC KENZIE.—Dr. Dannreuther's essay has made clear that the indications for therapeutic abortion at the New York Post-Graduate Hospital have been most carefully studied, and I share with Dr. Schumann the feeling of being in accord with Dr. Dannreuther's attitude and acts. It is my observation and belief, however, that in many hospitals therapeutic abortion has been viewed in less serious aspect, and the indications have not been as carefully considered before operation. Dr. Cosgrove's recent significant contribution to this topic points to the same conclusion.

It may be of interest to report here arrangements made at the Monmouth Memorial Hospital in Long Branch, New Jersey, to provide for therapeutic abortion in the occasional

case where definite irrefutable indications are present, but to eliminate the questionable cases where consultations to approve interference oftentimes have been such in name only. The Medical Board of the hospital has created a "Committee on Abortion." There are three members; the Chief of Staff who presides as Chairman, and one member each from the medical and obstetric departments. Each member is appointed for one year. The Committee meets upon call of the Chairman when there is need to consider the facts in a case to be presented by a physician who feels that abortion is necessary. If not already a patient in the hospital, the candidate for the abortion is expected to be in the hospital waiting room for questioning and examination. The decision of the Committee may be reserved until a laboratory test or other information has been obtained, but must be given within twenty-four hours of this time. Unanimous approval of the three members is required. Such approval, if voted, is to be recorded on a hospital chart before the pregnancy is interrupted. In the event that one of the members of the Committee wishes to present a case, his place is taken by another doctor selected from his department by the Chairman.

The formation of such a board of review has several advantages. It provides a meeting of minds with opportunity for discussion and decision upon the merits of each case. No physician is going to ask the Committee to consider a case which he has not carefully studied, nor about which he does not feel strongly. No woman will consent to be taken to the hospital for possible examination and interrogation unless she desperately feels the need for help.

In the twelve months preceding the establishment of this Committee, eight therapeutic abortions were performed. There have been no induced abortions in the nine months since the Committee has functioned. Two cases of early pregnancy with complicating conditions have been presented for study. In each case it was decided not to recommend interference.

DR. GEORGE H. RYDER.—Are we to limit therapeutic abortions to medical indications only? Shall we disregard entirely economic conditions? Are we to sanction therapeutic abortions solely for saving the lives of women at the time or shall we take into consideration their future health also?

What about hard-working women in poor health, with little money, who already have five or six children? Often we know that they do not have the strength to go through another pregnancy and to take care of the new babies in addition to the children at home. Shall we force them to go through additional pregnancies simply because we think that they will not die in childbirth?

In the Margaret Hague Hospital in Jersey City, with but four therapeutic abortions among seventy thousand pregnant women, it seems that the plea of such women must have been disregarded.

DR. HARRY ARANOW.—I have come to the conclusion that, on this question, after all, we are swayed by sentiment and that with all this discussion no one is convinced in the end. As Dr. Sehumann brought out, sentiment plays a role. For example, if a patient was threatened with illness or death if pregnancy progressed, I would permit her to have an abortion, whether the fetus was important or not, and whether the pregnancy had advanced to the second, third, fourth, or sixth month. I may be wrong in that, but after an obstetric practice of about thirty-five years I do not feel I myself am competent enough to decide whether the heart will stand labor, or whether a patient with tuberculosis or thyroid disease is going to get worse. I take it for granted that the man who advises me is honest and sincere and, while I can reserve decision, I am swayed by the opinion of the consultant most of the time.

DR. E. EVERETT BUNZEL.—Discussing therapeutic abortion in a general hospital, I believe that this calls for an answer to two questions: What is therapeutic abortion? What is a general hospital? Therapeutic abortion, in my opinion, is one in which termination of pregnancy is indicated to prevent the advance of disease or where there is a threat to the life of the expectant mother. A general hospital includes an obstetric division, which the Post-Graduate Hospital does not have.

I would like to know if there are any statistics of the number of patients admitted to this hospital who were refused therapeutic abortion once they were admitted. It seems to

mo that an obstetric opinion would be very essential, in addition to the opinion of a general medical man and a gynecologist. I have seen many patients with cardiac disease, particularly of the rheumatic type, who have been referred by outside agencies with a recommendation that therapeutic abortion be done. Granted that there is a history of rheumatic heart disease and that the patient shows evidence of mitral stenosis, how do you determine, as the essayist brought out so well, whether this particular patient is one who deserved emptying of the uterus? It seems to me that in most of the instances where there is an element of doubt, and certainly that exists in at least 50 per cent of patients admitted to a prenatal clinic, such patients should be admitted to the hospital for observation and study to determine the cardiac reserve.

I agree with Dr. Dannreuther that one of the most important things is the history which we get in these cases and I for one wish to go on record as saying that I am perfectly willing to recommend therapeutic abortion in a patient with rheumatic heart disease if there is a history of a period of decompensation within one year prior to the onset of pregnancy. You can be almost sure that as the pregnancy progresses, and as this living tumor increases in size and produces pressure on the diaphragm, with a decreasing amount of thoracic space available for respiratory use, that the patient will become more and more dyspneic, cyanotic, and orthopneic. She is much more apt to experience greater difficulty as pregnancy advances, unlike tuberculosis where the lesion is not much increased, if at all, during the course of pregnancy.

I believe that electrocardiographic tracings are essential, that the two-meter plate is important, as well as determination of kidney function.

In the cases that were aborted at the Post-Graduate Hospital nothing was said about the method of interruption; nor the time when the pregnancy was interrupted. Nothing was said as to how many patients were subject to hysterotomy and sterilization when the condition was so far advanced that it was thought these patients should never again become pregnant; whether the patient was able or willing to use contraceptive devices. There were four cases in which pregnancy was interrupted because of a history of epilepsy. I don't know just why epilepsy should constitute an indication for therapeutic abortion. The neurologists are very much at odds as to whether that is a hereditary disease. They admit that during pregnancy a patient with epilepsy is far better than before, but that the epileptic seizures will recur following pregnancy. Interruption of pregnancy does not cure epilepsy.

So far as the thyroid operations that Dr. Heyd referred to, I agree with him absolutely. We have had several cases in which partial or total thyroidectomy was done in the early part of pregnancy and I know of only one instance in which spontaneous abortion followed thyroidectomy. We do not know that this particular patient would or would not have aborted anyway. Certainly the weight of evidence would be in favor of assuming that the thyroidectomy was not responsible for the so-called miscarriage which occurred following the operation.

DR. DANNREUTHER (Closing).—I would like to emphasize that, when I originally compiled the statistical data, it was done only to secure the figures indicating the frequency of therapeutic abortions during a ten-year period. Although no charts were inspected or reviewed, the total number of cases, 84, seemed creditably small. Perhaps it was higher than it should have been. In this group of cases, many of the abortions were done before the adoption of the existing hospital rules, and possibly some of them would be refused today.

Personally, I have seen a larger percentage of the candidates for therapeutic abortion since these rules have been in effect than I did previously. However, I cannot tell Doctor Bunzel how many patients were refused a therapeutic abortion, and know of no way whereby such information could be secured from the record room. It would also seem an almost impossible task to prove exactly to what extent a therapeutic abortion contributes to the prolongation of life expectancy. It would be wrong to contend that a therapeutic abortion can cure epilepsy or a brain tumor or any other disease, and I had no intention of implying any such thing. But it may protect the health and lengthen the life of many patients whose existence might otherwise be much more distressing.

## INTERPRETATION OF THE PATHOGENESIS OF PELVIC INFECTION AS DETERMINED BY CORNUAL RESECTION\*

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IT IS generally accepted that the primary infecting organism in most cases of salpingitis has been the gonococcus, in spite of the fact that at operation cultures of the tubes are either sterile or reveal other organisms. This raises the following questions:

1. Does the gonococcus prepare the tube for infection by other organisms, or is a tube infected with the gonococcus more susceptible to secondary invasion?
2. Does the gonococcus disappear from the tube when these secondary invaders appear, or are they present but overgrown by other organisms?
3. How did these secondary invaders reach the tube?

These are the questions that trouble the student of pelvic inflammatory disease. Before they can be answered certain fundamental limitations in the present knowledge of the bacteriology and immunology of gonococcus must be reviewed.

A. Cohn and I. Grunstein,<sup>1</sup> in their discussion of the cultural methods of diagnosing gonorrheal infection, state: "little is known of the actual facts interfering with the accuracy of the bacteriologic methods, although various explanations have been advanced." One view stressed by the Gonococcus Research Unit emphasizes the fact that biologic changes in the infected tissues and their resulting action on the organisms may cause anatomic or immunologic reactions which decrease the number and viability of the gonococci.

Other investigators (Van Slyke, C. J. Thayer, J. Durward, and J. F. Mahoney)<sup>2</sup> believe that the limitations of the culture diagnosis is due chiefly to a lack of sensitivity of our present culture media. "Experimental evidence indicates that a minimal number of viable organisms must be present before a culture can be obtained. With the available culture media this medium represents a very large number of organisms. The ideal medium would be one sensitive enough to promote growth when a single viable organism is present in the pus specimen."

The fact that the gonococcus, when confined in a closed space like the tube soon dies, whereas when it is contained in the cervix where it has unrestrained secretions retains its virulence for a long time, has been accepted by most authorities.

Yet Curtis<sup>3</sup> states that "combined laboratory study and clinical experience formerly led me to the deduction that gonorrheal infections of the cervix are unusually persistent. This belief appears to require some modification. Consequent re-infection accounts for more of these cases than were evident in my earlier experience, and Gram negative diplococci, other than the gonococcus, have gradually been found to occupy a somewhat more important role in the bacteriology of chronic endocervicitis."

\*Presented to the Obstetrical Society of Philadelphia, Nov. 1, 1945.

One attack of gonorrhea in the cervix does not set up any immunity. There may, however, be an acquired local immunity against a certain strain of gonococci with which the patient and her consort are persistently infected. As a result, the patient does not develop the symptoms of an acute infection every time she comes in contact with this particular strain. Does this same local immunity hold in the tube? This is very doubtful, because it would appear that in the tube, with the disappearance of symptoms, the gonococci die; and, as there is no natural immunity against the gonococcus, when a reinfection takes place from the cervix along the endometrium to the tube, it is practically the same as if a new infection set in.

It has long been known that gonococci as well as streptococci may remain dormant in the cervix for years. Curtis<sup>4</sup> has shown that approximately 30 per cent of all patients with chronic purulent leucorrhea are carriers of virulent streptococci.

Any attempt to study the bacteriology of the infected tubes must of necessity take into consideration the fact that today it is unusual to operate on any patient during her period of active disease. It is customary to wait until the temperature and blood count have been normal for at least two weeks. As a result, the acute process has almost always subsided and the operation takes place on tubes in the subacute or chronic state.

A further complication to enter the field of the bacteriology of the infected tube is the inhibiting effect on the growth of the gonococcus and other organisms by the normal antibodies produced in the tissues, the sulfonamides and penicillin.

The fate of the gonococcus in the tube has long been under discussion. If the gonococcus invades the wall of the tube, does it reproduce in the wall of the tube as a gonococcus, or does it change its morphology and no longer appear as a diplococcus, as suggested by Casper.<sup>5</sup> With the advent of other organisms in the tube does the gonococcus disappear or do these other organisms, streptococci, staphylococci, etc., so completely overgrow the gonococci that the latter cannot be isolated from the infected tube?

The bacteriology of the infected tube has been studied in many gynecologic clinics and there has been an almost unanimity of opinion that organisms (gonococci, streptococci, staphylococci, etc.) cannot be cultured from the infected tubes in any large percentage of cases if one waits two weeks after the temperature has subsided.

Curtis<sup>6</sup> found that, in cultures made from over 200 thoroughly ground Fallopian tubes, it was rarely possible to obtain the gonococcus longer than two weeks after the disappearance of fever and leucocytosis. Studdiford, Casper, and Seadron,<sup>7</sup> found organisms identified as gonococci in the tubes of 66.6 per cent of 24 cases of salpingitis investigated bacteriologically, in spite of the fact that none of them were in the acute stage of the disease. Most of the patients had been afebrile for two weeks. Cohn and Grunstein<sup>1</sup> examined the operative material of 19 patients from Bellevue Hospital. Bacteriologic material for smears and cultures were taken from 14 inflamed Fallopian tubes, seven ovaries, two uterine cavities, and from a ruptured tuboovarian abscess. After surgical removal, the different organs were opened, and any exudate present on the sur-

face of the mucous membrane was taken up by a sterile swab which was immersed in peptone water. The mucous membrane was then scraped with a sterile knife in order to obtain exudate from the deeper layers of the inflamed tissue. In some cases pieces of tissue were excised, immersed in peptone water, and ground up in a mortar before final inoculation into culture media. All of this operative material yielded negative bacteriologic findings.

A study of the bacteriology of infected tubes was undertaken at Harlem and Beth Israel Hospital. At first only the cornual portions of the tubes removed at operation were used for culture. These cultures were almost always sterile and histologic examination of the tissue removed at operation frequently showed no pathologic change. As a result, for this study tubes were removed in toto and subjected to smears and tissue cultures.

*The Technique Used for Culturing Tubes\** (Beth Israel Hospital).—The surgeon removed the specimen (the uterus with tubes and ovaries), and placed them in a sterile specimen jar. The technician, with sterilized instruments, separated the tubes from the ovaries and uterus and placed each tube in a sterile Petri dish and opened the tube longitudinally with sterile scissors. The lining of the tube was then scraped with a strong loop or wooden applicator. Cultures were then made on chocolate agar plates and a smear taken for study. A portion of the proximal and distal part of the tube was excised and placed in separate Petri dishes to be used for tissue culture. The specimens were then carried to the laboratory and cultured on different media.

In the laboratory the slide was stained (gram's technique) and examined microscopically. Each of the remaining parts of the tube were scraped thoroughly with a loop and cultured on chocolate agar, endo-agar, blood agar and Fortner plates (for anaerobes). The tissue particles were taken from the Petri dishes and placed in a fluid media such as thioglycollate, plain broth, and proteose peptone. All media were placed in a 37° C. incubator and the chocolate agar plates were put in a 20 per cent CO<sub>2</sub> atmosphere. After twenty-four hours all media were checked. Those with growth were smeared and subcultured. Proteose peptone cultures were transplanted to chocolate plates, even if no viable growth was present. All media were observed as follows: endo-plates for forty-eight hours, chocolate agar and anaerobic plates for three days. The tissue in proteose broth was kept eight days and subcultured again for final examination. All positive cultures were subcultured for isolation and final determination.

In the first series 140 cases were studied, 108 cases gave negative cultures, 5 cases were contaminated, and 27 cases gave positive cultures. These were as follows: *Salmonella typhi murium*, 2, *Streptococcus hemolyticus*, 5, *Bacterium coli*, 6, *Streptococcus viridans*, 11, *Bacterium lactis aerogenes*, 1, *Micrococcus gonorrhoeae*, 2.

A second and independent bacteriologic study was then undertaken in the bacteriologic department of Harlem Hospital.

*Technique Employed in the Bacteriologic Study of the Fallopian Tube.*†—As soon as the portion of the tube was brought to the laboratory it was placed in a sterile Petri dish. The mucous membrane was exposed and scraped with a

\*This work was aided by a grant from the Greater New York Fund.

†This work was aided by a grant from the Gynecologic fund of Beth Israel Hospital.



strong wire loop and the material cultured. Pieces of the tissue were also cultured. All material was placed on the following media:

1. Blood agar
2. Thioglycollate broth (Brewer)
3. Brewer's anaerobic agar
4. Proteose No. 3 agar with hemoglobin and plasma enrichment—  
plasmahem agar.

A smear was also prepared from the scrapings of the tissue. This was stained by means of Gram's technique. The presence or absence of microorganisms and pus cells was recorded.

The blood agar plate, thioglycollate broth, and Brewer's anaerobic plate were placed in the incubator at 37° C. The plasmahem plate was placed into a 10 per cent CO<sub>2</sub> atmosphere, incubated at 37° C. for thirty-six to forty-eight hours, and then examined for gonococci. Suspicious colonies were subcultured for purity and then examined for gonococcal, physiologic, and morphologic properties.

A Gram negative diplococcus was recognized as a gonococcus by its:

1. Typical colony formation
2. Failure to grow at room temperature
3. Ability to ferment dextrose and not maltose.

The blood agar plate and Brewer's anaerobic plate were examined daily for four days and the thioglycollate broth for ten days. Obviously as growth was visible, the usual bacteriologic procedures were used for the isolation and identification of microorganisms found.

In this second series 76 cases were studied

Sixty-four cases gave negative cultures.

Twelve cases gave positive cultures.

The positive cultures were as follows:

Staphylococcus aureus hemolyticus	6
Staphylococcus albus	1
(Microaerophilic) gram negative bacillus	1
Nonhemolytic Streptococcus	1
Gram negative diplococcus not gonococcus	1
Gonococcus	2

In no instance were microorganisms demonstrable on smears, although the smear on four occasions showed 2 and 3 plus pus. These two studies verify the findings of Curtis,<sup>6</sup> that, when the acute symptoms subside, organisms which can be cultured have disappeared from the tube. If this is true, then how does the second, third, or fourth attack of salpingitis occur? Is it a lighting up of a latent or dormant infection in the wall of the tube which cannot be demonstrated by our present bacteriologic methods, or is it a new infection from without the tube (i.e., male carriers, cervix, etc.)?

For the past eight years it has been the custom at Harlem Hospital not to remove pus tubes. The tubes were only removed when the ovary was involved (tuboovarian abscess or ovarian abscess). Instead, the continuity of the tube, uterus, and cervix was broken by resecting the cornual end of the tube and leaving the rest of the tube in situ. The reason for this procedure was that, as demonstrable organisms had disappeared from the tube after the temperature



had been normal for two weeks the tube could not reinfect itself, but was infected from without through the cervix and uterus. Whether this occurred from an infected consort or an infected cervix did not matter.

If this concept is true, then leaving in the infected tube and breaking its continuity with the cervix should prevent reinfection of the tube. If, however, this concept is not true and reinfection of the tube occurred as a "lighting up" of a latent or dormant infection in the wall of the tube, then breaking the continuity of the tube with the cervix should not prevent attacks of recurrent salpingitis.

Cornual resection<sup>10-13</sup> has been carried out in over 1,000 cases with a follow-up of over eight years, and in no instance have we seen or heard of a reinfection occurring in any of these resected tubes. Since all the patients in Harlem Hospital are indigent patients, they, of necessity, when sick, must reapply to Harlem Hospital or to some other City Hospital for admission. None of these cases have been readmitted to Harlem Hospital with a recurrence of the salpingitis. We have not heard of any of these cases being admitted to any other hospital for treatment for pelvic inflammatory disease after cornual resection. We have, however, had an opportunity to reoperate on six of these patients who subsequently developed fibroids or ovarian cysts as a complication. In all of these cases the tubes were removed at the second operation for study. In no instance were we able to demonstrate in these tubes, removed nine or more months after the cornual resection, any histologic evidence of acute or chronic inflammatory disease.

This brings us back to our original questions:

1. Does the gonococcus prepare the tube for infection by other organisms, or is a tube infected with the gonococcus more susceptible to secondary invasion?
2. Does the gonococcus disappear from the tube when these secondary invaders appear, or are they present but overgrown by other organisms?
3. How did these secondary invaders reach the tube?

There is no doubt from the material studied in the Harlem Hospital Out-Patient-Department that the primary infecting organism in most cases was the gonococcus. Patients entering the hospital in their primary attacks of salpingitis demonstrate by smear and culture the gonococcus from the cervix in a fairly high percentage of cases. Primary streptococcus or staphylococcus infection of the tube may occur, but is infrequent.

It is evident from this study and those of a majority of other observers that in patients who have had frequent attacks of salpingitis, the gonococcus had disappeared from the tube, and other organisms have replaced them. There is no question from bacteriologic and pathologic studies that these secondary invading organisms play a prominent role in pelvic inflammatory disease.

It would therefore appear that the gonococcus is either overgrown or replaced by these other organisms. As primary streptococcus and staphylococcus, etc., infection of the tube is infrequent, and as these organisms play such a prominent role in pelvic inflammatory disease, is it not probable that the tube infected with the gonococcus is more susceptible to these secondary invaders?

It has long been generally accepted that the gonococcus ascends from the cervix through the cavity of the uterus to attack the tubes from within (luminal infection), whereas the streptococcus and staphylococcus are presumed to go by way of the lymphatics and attack the tubes from without (mural infection).

Is the gonococcus the only organism that attacks the tubes from within? Is it not probable that when circumstances are appropriate—low resistance, endometrial reaction, instrumentation, etc.—the streptococci and staphylococci, which are present in the crevices of a great many women, enter the uterus and thus gain access to the tubes? This probably is true in spite of the fact that it has long been taught that the streptococcus and staphylococcus are lymphatic organisms and extend through the broad ligaments to the wall of the tube and produced a perisalpingitis. Primary luminal streptococcus, staphylococcus, and coli bacillus infections of the tube usually produce a generalized peritonitis (Falk and Blinick),<sup>12</sup> although one must admit the possibility of a low-grade primary infection without peritonitis. Black-Schaffer<sup>13</sup> studied the tubes removed from 50 patients at varying intervals during clinically normal puerperia. In 19 cases he found acute salpingitis. The mucosa of the tubes was the stratum most prominently involved. In those tubes which showed the most advanced lesions, aggregates of polynuclear leucocytes were seen in the edematous hyperplastic muscularis and subserosa. In no case was the peritoneum involved. Since the inflammation probably spread along the endometrium to the mucosa of the tubes, he assumes that an unrecognized postpartum endometritis must have existed.

In patients who have had recent attacks of recurrent salpingitis, we have been able to demonstrate in sections of the fundus of the uterus evidence of recent inflammation, leucocytic infiltration, etc. Bell<sup>14</sup> stated that many of his cases of chronic salpingo-oophoritis were associated with chronic infection of the fundus of the uterus. Beck, quoted by Polak,<sup>15</sup> stated that a microscopic study showed that infection from the tubes spreads into the muscularis of the uterus to a considerable extent.

It is our belief that this infection, whether gonorrheal, streptococcal, or staphylococcal, did not come from the tube to the fundus of the uterus, but that the infection began at the cervix, extended upward to the fundus of the uterus and then outward to the lumen of the tubes. If this is not true, how else can we explain the absolute disappearance of the infection in the tube on performing a cornual resection. If the tubes reinfect themselves, why did we not have a single case of recurrent salpingitis with fever in a patient on whom the only procedure was a resection of the infected tube from the cornua of the uterus, thus breaking its continuity with the cervix.

### Conclusions

1. The fact that the gonococcus is the infecting organism in most cases of primary salpingitis is accepted.
2. The question as to whether the gonococcus prepares the tube for subsequent infection by other organisms is discussed.
3. The fact that the streptococcus, staphylococcus, and other organisms may ascend through the uterus to the tubes is discussed.

4. The recovery of organisms—gonococci, streptococci, and staphylococci—from infected tubes is infrequent.

5. Cornual resection prevents reinfection of the tubes.

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1 WEST EIGHTY-SIXTH STREET

### Discussion

DR. EDWARD A. SCHUMANN.—This essay opens a wide field for discussion, aside from the specific questions Dr. Falk has asked and answered.

Gynecologists are agreed that the gonococcus is the most common infectious agent in the causation of pyosalpingitis, and the modern conception of its subsequent fate in the tube has been well stated by the essayist. Gonorrhea is now generally considered to be a self-limited disease in both sexes, chronicity being somewhat doubtful except possibly (and only possibly) in the cervix. Residual lesions are, of course, common stricture and prostatic involvement in the male, agglutination of the tubal mucosa, and peritubal adhesion in the female. However, the lighting up of a so-called latent gonorrheal infection seems to be an erroneous conception, it being much more probable that reinfection has occurred. The original work of Curtis has never been disproved and showed conclusively that the life of the gonococcus in the tube was comparatively short.

Secondary infection by pyogenic bacteria frequently follows specific infection in various organs, the kidney, gall bladder, and tonsil being commonly so affected.

To me the most interesting part of Dr. Falk's paper was his statement, supported by a large number of case histories, that secondary and subsequent infections of the Fallopian tubes did not follow an initial healed salpingitis when the uterine cornua were resected and the tubal mucosa thus cut off from the uterine cavity.

This would seem to prove, by simple clinical observation, that tubal infections travel along the endometrium and reach the tubes by the cornual passages and not by way of vascular or lymph channels.

The quoted work of Black-Schaffer is of great importance in this connection as has been stated. This author studied the tubes removed from 50 patients at various intervals during clinically normal puerperia. I assume that these specimens were mostly obtained after postpartum sterilization procedures, and in almost 40 per cent of these cases he found acute salpingitis, although in none of them was the peritoneum involved. This certainly seems to point to direct infection by continuity rather than a lymph- or blood-borne invasion.

With regard to repeated attacks of salpingitis, it seems reasonable that there are either frank new infections by the gonococcus or that certain pyogenic bacteria, gaining access to the tubes via the uterine cavity, are able to develop readily among the debris of the original infection, since all tubes once the seat of a salpingitis reveal, upon close examina-

tion, little crypts where the mucosal papillae have become agglutinated as well as certain areas of ischemia form tiny infarcts, together with areas of inhibited lymph flow, all of which form excellent fields for bacterial growth.

DR. ROY W. MOHLER.—I have had occasion a number of times to do cornual resections with about the same technique that Dr. Falk has described. I have observed very carefully for a number of years four or five patients on whom I have done cornual resections. Each patient has been clinically well during the whole period of observation. The patients were girls who had recurrent pelvic infections. I was very anxious in these particular patients not to remove the ovaries. Against my better judgment in the first few cases, I did cornual resection, and my subsequent observations have indicated that the patients are clinically well.

DR. FALK (Closing).—I was asked about the advantage of leaving the tube in situ. I would prefer to state the disadvantages of removing the tube. Every year we see at least a dozen patients with ovarian cysts whose tubes have been removed and in whom the ovarian blood supply has been interfered with. Intestinal injury is not an unusual complication of salpingectomy. Cornual resection is a simpler operation with fewer complications.

Dr. Schumann's question with regard to the demonstration of the gonococcus in the endometrium; to demonstrate the gonococcus in the endometrium it is necessary to remove the uterus during the primary acute attack which is not done today. Wertheim, however, did demonstrate the gonococcus on the endometrium about 40 years ago. In answer to Dr. Outerbridge's question, we have left in pus tubes with a diameter of four centimeters. The first case operated upon had pus tubes three centimeters in diameter. A cornual resection was performed and she left the hospital in two weeks, going back to work. We were able to follow her very carefully. The mass entirely disappeared. We are hoping to have one of these patients return as a sterility study. We are anxious to see if we can reimplant the uterine end of the tube into the cavity of the uterus and have a pregnancy result. We doubt it very much as the fimbriated end of the tube will probably be closed in most of the cases.

# THE CLINICAL DIAGNOSIS OF VARYING DEGREES OF UTERINE CONTRACTION RINGS\*

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IT IS a great honor to be invited to present the first paper under the "C. R. Hannah Memorial Lectureship." I fear that it will fall far short of being worthy of the founder of this society, the outstanding teacher, and the intimate friend of most of us present. Dr. Hannah was dynamic. He liked one to argue his point, right or wrong, with firm conviction. He also wanted one to be brief. I trust his soul will not be disquieted by this presentation.

I have chosen the subject, "The Clinical Diagnosis of Varying Degrees of Uterine Contraction Rings," because Dr. Hannah was interested in contraction rings, and because delving in the subject has been very interesting to me. Moreover, I am convinced that the delay in some otherwise normal labors is often caused by sublinical uterine rings. In two former papers<sup>1, 2</sup> read before our State Society, various phases of the subject, especially etiology and treatment, have been discussed. While these papers did not offer any great contribution to the literature, they have stimulated interest in ring dystocia among some of our doctor friends, as will be seen from Table I.

TABLE I. INCIDENCE OF CONTRACTION RING DYSTOCIA AS DETERMINED IN DIFFERENT INSTITUTIONS

<i>Drs. Johnson and Johnston:</i>		
10,000 Consecutive Cases		
Contraction Rings		126
Incidence 1.26% (1 in 80 Deliveries)		
<i>St. Joseph's Maternity:</i>		
24,524 Consecutive Cases		
Contraction Rings		97
Incidence 0.39% (1 in 254 Deliveries)		
<i>Memorial Hospital:</i>		
10,461 Consecutive Cases		
Contraction Rings		28
Incidence 0.26% (1 in 402 Deliveries)		

In this table it is noted that in our practice ring dystocia occurred once in every 80 deliveries; whereas at St. Joseph's Maternity where most of our cases are delivered it occurred only once in every 254 deliveries; and at the Memorial Hospital it occurred once in every 402 deliveries. Obviously, these apparent differences in incidence of this complication of labor are not real but represent varying degrees of interest in or awareness of it.

A few introductory remarks about uterine rings might be in order. The occurrence of a physiologic retraction or contraction ring at the junction of the

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upper and lower uterine segments is well established. Whether it forms during the last trimester, just before, or during labor, is still a disputed question. Williams,<sup>3</sup> specimen of a seven months' pregnancy shows the ring or ledge well defined. Beck's<sup>4</sup> drawings perfect the lower uterine segment and the physiologic ring as the first stage of labor progresses.

Proceeding to the realm of pathologic rings, one is confronted by a maze of bewildering terminology and assumptions. Less confusion would result if the authors of our acceptable textbooks could agree on a standard nomenclature, deleting or leaving in small type all duplications of terms. There are, according to them, retraction rings, contraction rings, and constriction rings. The student is told that the two former may be temporary or permanent, passable or impassable, reversible or irreversible. One author refers to Bandl's ring as a progressing process of retraction at the site of the physiologic ring; claims that the ring moves gradually upward as the upper segment thickens; that the lower segment becomes markedly thinned, and it is in this segment that rupture of the uterus takes place; and that this process occurs only in obstructed labors. DeLee and Greenhill,<sup>5</sup> citing Rudolph as their authority, call the ring a constriction ring because it is essentially a functional constriction which may occur at the external or internal os, at any level of the lower uterine segment, at the site of the physiologic ring, or at any level of the upper uterine segment. They use the same authority for claiming that constriction rings may be atavistic, representing segmentation of the uterus—as found in Rodentia, Carnivora, and Ungulata; that the cause of the ring formation is unknown, and that there is no evidence that early rupture of the membranes, bags, drugs, malposition, malpresentation, or intrauterine manipulation are causative factors.

The foregoing is confusing to medical students and doctors as well. With or without good obstetric authority, *Standard Nomenclature of Diseases and Operations* has taken the first step toward clarification. In those hospitals which have adopted the Standard Nomenclature, rings are now all contraction rings. The terminology used in this paper has been made statistically and otherwise to conform to Standard Nomenclature. In former papers the term Bandl's retraction ring has been preferred, since (a) the term has quite general significance, and (b) in answering the question "is the constriction now present in the uterus due to constriction, contraction, or retraction of the muscle fibers?" it has been more natural to think of the constriction or ring as being due to a process of retraction. But in spite of our present-day confusion, we have good authority, in addition to our own personal experience, to be convinced that rings occur in both obstructed and unobstructed labors and, when present, are always a formidable complication to the progress of labor.

In the first group of cases, obstruction to the passage of the fetus causes development of the contraction ring, while in the second group the contraction ring causes obstruction to the passage of the fetus. In the first group the ring formation would be dependent on the degree of obstruction to labor. In the second group, and it is this group with which this paper is mostly concerned, all cases might be divided by their clinical courses into mild and severe. The mild

cases would comprise all labors where other causes of dystocia could be eliminated and which greatly exceeded the normal duration, but which terminated spontaneously or by simple delivery procedures under the lower limit of prolonged labor, i.e., thirty hours. The severe cases would comprise labors which greatly exceeded thirty hours and terminated under surgical anesthesia by more involved delivery procedures. There are varying degrees of toxemia, placenta previa, premature separation of the placenta, et cetera. If contraction ring dystocia in unobstructed labor is an entity, it appears reasonable to suppose that it also might occur in varying degrees even down to a definitely sub-textbook variety.

In reviewing the literature up to 1935, Rudolph reported that in his 371 collected cases the maternal mortality was 15 per cent; the fetal mortality, 46 per cent; operative incidence, 97 per cent. In 1941 the writer reported 105 cases of Bandl's ring occurring during 7,339 labors in the practice of Johnson and Johnston. Operative interference was 100 per cent, maternal mortality nil, fetal mortality 4.7 per cent. It seems obvious that, in view of these great discrepancies, Rudolph collected from the literature the most severe and perhaps neglected cases. It is hoped that our cases were not neglected, and that delivery was effected as early as circumstances warranted. His were the grave cases; ours the milder ones, but nevertheless offering a definite delay in the progress of labor, and susceptibility to the diagnosis of ring dystocia. It is these varying degrees of ring dystocia, or milder cases, which, if observed carefully, cause one to become more ring conscious, with the result that the true cause of the unreasonable delay in labor is detected. I feel that anything tending to popularize this concept will be of benefit by way of earlier interference, and thereby reduce maternal and fetal mortalities.

My experience with ring dystocia is that the textbook Bandl's ring must occur in obstructed labors, because it merely represents the ultimate result of the mechanics of expulsion in a uterus which has gone all-out to empty itself against obstruction. But unobstructed labors are greatly in the majority, and in a small percentage of these ring dystocia develops. It is also apparent that the complication may develop at any time from the beginning of labor to very late in the first stage, or even during the second stage. No doubt some few of us, in order to get a little football insurance for the game at 2:30 P.M., have ruptured the membranes at 8:00 A.M. Saturday in a normal case with 5 cm. cervical dilatation. Then, to our bitter disappointment, we not only had to miss the game, but also divine worship at 11:00 A.M. Sunday morning.

We cannot agree with Rudolph that early rupture of the membranes is not a predisposing factor in the development of uterine rings. It has happened too often in our cases to be ignored. In fact, where the membranes have ruptured before or early in labor, and subsequent cervical dilatation has not kept pace with the frequency and severity of the uterine contractions, we have become suspicious of a developing ring, and often this suspicion has been warranted. But there is much to support Rudolph's contention that temporary contraction rings are functional, for some of our severe cases have had subsequent labors without recurrence. Also, while deep surgical anesthesia is required to relax

most rings, lesser degrees of anesthesia, good sedation, or adrenalin chloride may relax the milder forms. At least, relief is sometimes afforded by these milder measures.

Apology is offered for being unable to present anything really new in the clinical diagnosis of ring dystocia. However, it may be worth while to refresh our minds on the cardinal symptoms and signs, and then to visualize these signs in the accompanying diagrams. For this purpose ring dystocia developing early in the first stage of labor is best suited. Many of these patients give a history of the mother having had a long labor. (The mother always claims there were no good doctors in those days.) Also, not a few of these patients are introspective and have looked to the very last detail of good prenatal care. As a class, if there be such, they might be called hypertonic introverts. Labor starts quite normally (Fig. 1) and then after a few hours, the complaints of the patient become urgent because of the colicky nature of the pains. Rectal examination (Fig. 2)

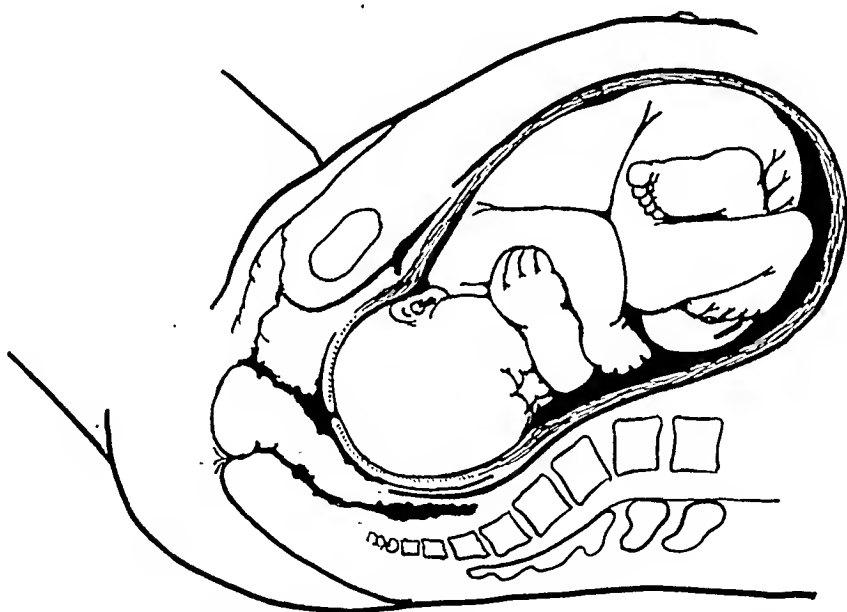


Fig. 1.—Onset of labor in primipara at term. Head engaged, cervix ripe, membranes intact. Physiologic contraction ring present.

satisfies the inexperienced that the complaints are not in accord with the progress of labor and the patient is in for a good sound scolding. Even the pallor and the small beads of perspiration mean little or nothing to him. The experienced physician, after such rectal examination, on the other hand, is conscious of what is taking place and is moved to sympathy. Immediate relief is ordered along with words of understanding and encouragement. May I state here that the popular saying and belief, "the cervix will *always* dilate when the labor pains are adequate," should be changed to "the cervix will *always* dilate when the labor pains are adequate *but only very slowly in unobstructed labors where a contraction ring is forming or has formed.*"

After a few hours of rest produced by sedation, the battle is on again, and as the hours pass the colicky character of the pains increases, the patient holds her hands over the uterus because it has become sensitive and she wants to pro-



teet it from the hands of nurses and doctors. She may now show some signs of fatigue, and the urgency of another period of rest becomes apparent. A vaginal examination may now show the station of the head to be slightly higher than noted earlier in labor. Some increase in cervical dilatation (Fig. 3) has taken place, possibly 2 or 3 cm., with soft, somewhat edematous cervical edges. The middle finger of the examining hand (Fig. 4) is inserted rather

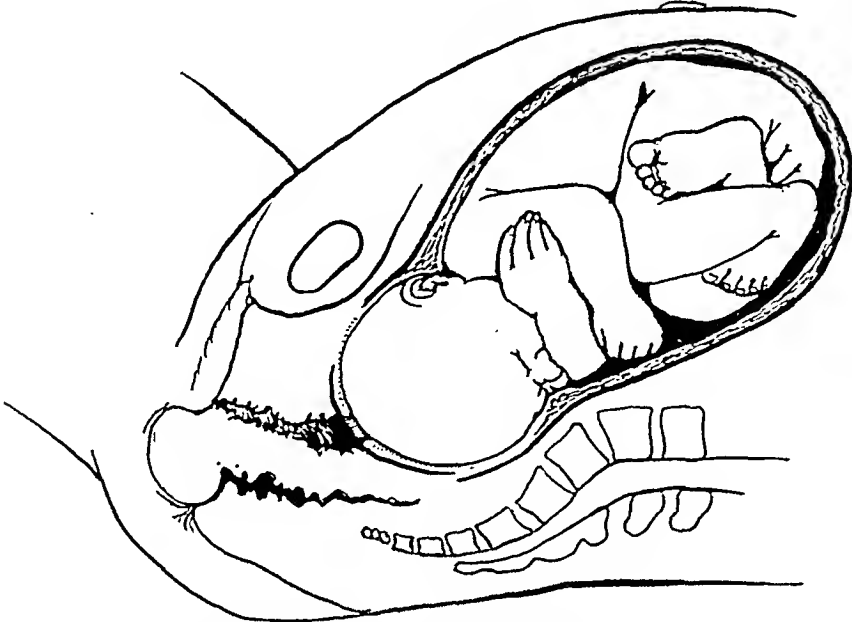


Fig. 2.—After several hours of labor, cervical dilatation does not correspond with the duration of labor nor the severity of the pains. The physiologic contraction ring is more marked.

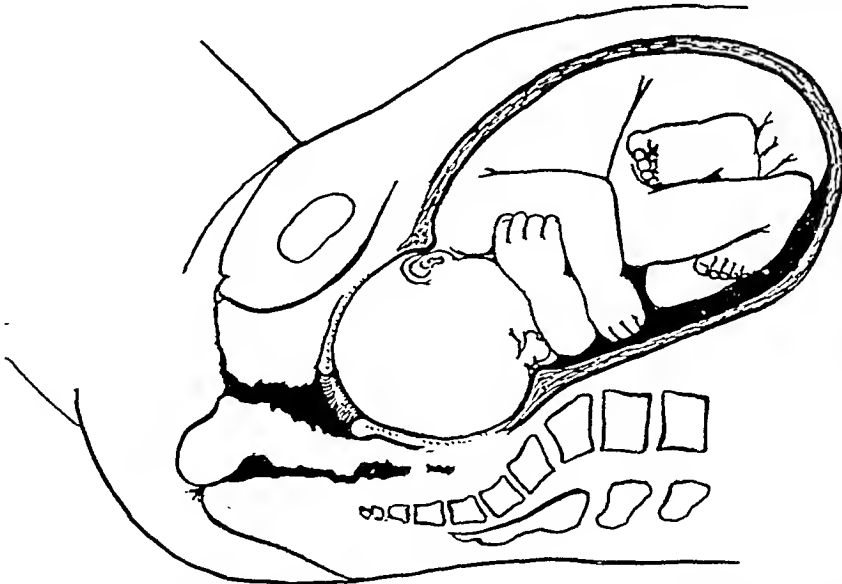


Fig. 3.—Cervical dilatation increased to 3 to 4 cm., with soft and edematous edges. The station of the head is slightly higher. The physiologic ring has become a pathologic contraction ring.

deeply between the cervix and the head. The other hand is placed on the body of the uterus and kept there until a strong contraction is felt, when the impact on the examining finger is sensed as very weak. (Fig. 5 suggests a simple method of sensing pressure of uterine contraction.) The fetal head is found to be mov-

## Labor room diagnosis

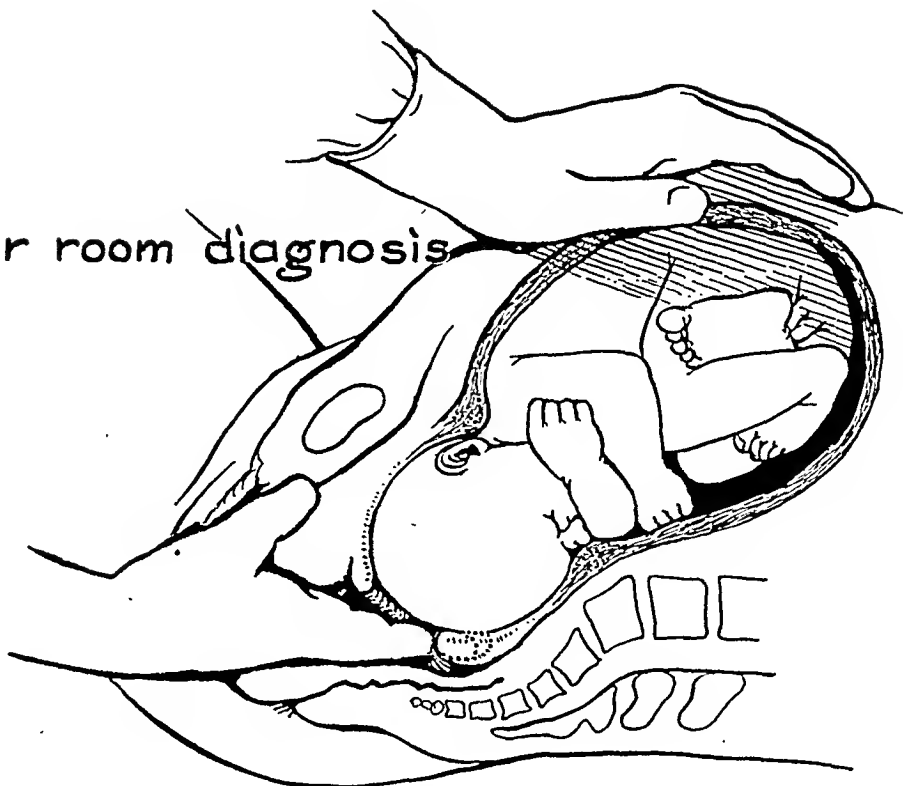


Fig. 4.—After several hours more of labor the cervix is dilated 4 to 5 cm., and is more edematous. Vaginal examination shows that pressure of uterine contraction is not imparted to the examining finger held between the cervix and fetal head.

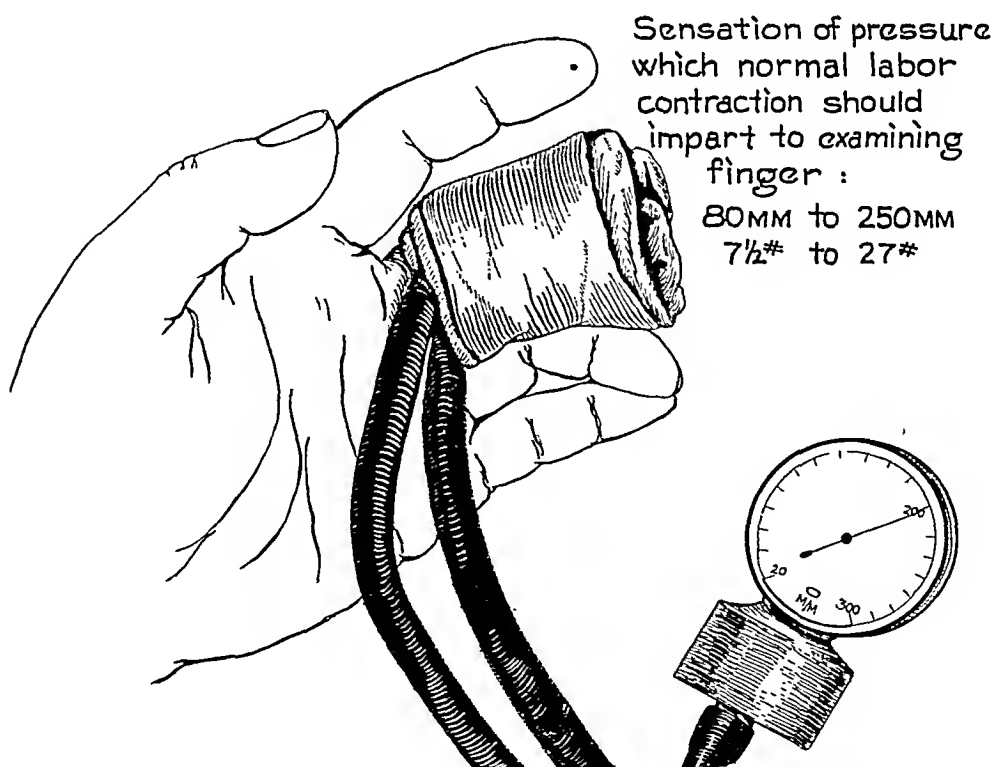


Fig. 5.—This shows the use of the sphygmomanometer to sense the amount of pressure of uterine contractions. This ranges from 7½ pounds (80 mm.) to 27 pounds (250 mm.).

able or loose in the pelvis. There can now be little question about the diagnosis. With the periods of rest and labor, thirty or more hours have now elapsed. The patient begs for a cesarean section. She knows that any medicine given her will afford only temporary relief, and she senses the utter futility of being able to deliver herself. Vaginal or rectal examination now may show the cervix 4 cm. dilated (Fig. 6), soft and edematous. The patient is now ready for delivery, and more than likely so per vaginam.

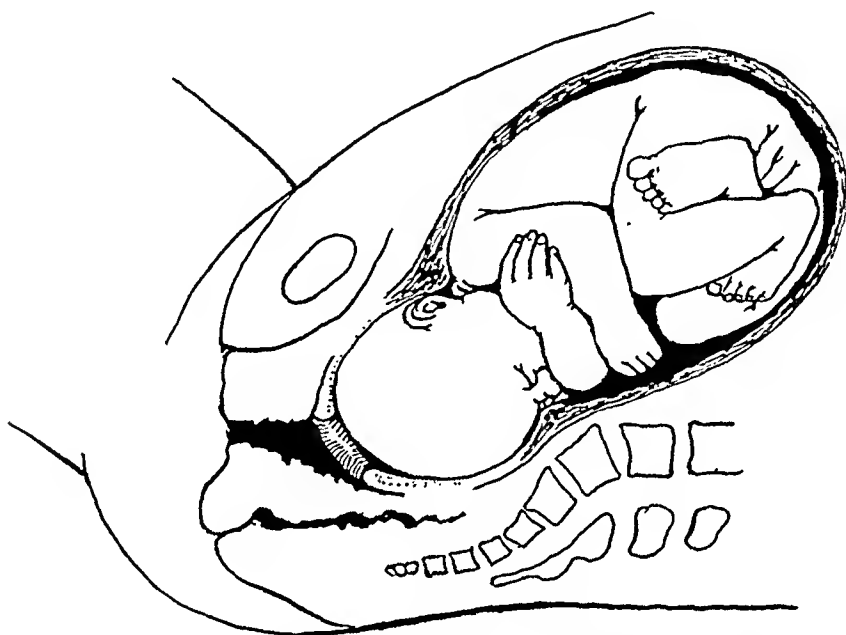


Fig. 6.—Cervix dilated 4 to 5 centimeters. Labor over thirty hours. Station of head slightly higher. Ready for delivery per vaginam.

Fortunately, the case with which these cases may be delivered is in marked contrast to the difficulties and anxieties suffered by both the patient and doctor during the long hours of labor. This is easily explained when it is realized that in unobstructed ring dystocia only the contraction ring prevents the passage of the child, and therefore the only requisite to easy delivery is relaxation of the ring. With the condition of the cervix as just described, and the duration of labor well over thirty hours, the patient is prepared for delivery. The outer gate of the birth canal is opened with the episiotomy of choice, and the hand is carried deep into the vagina to iron out or stretch the posterior pelvic fascia and the underlying portions of the levator ani muscles. This is advisable, since the fetal head has not been forced against these structures to condition them for the passage of the child. The edematous cervix is now felt as a drape covering the most dependent portions of the presenting part. It does not require manual dilatation as one thinks of the term, because the cervix generally brushes aside by merely opening and separating the fingers of the operating hand. The latter is now carried upward posteriorly between the lower uterine segment (Fig. 7) and the fetal head for the purpose of making an accurate diagnosis of position, and also to determine the presence of any loops of cord below the ring. At this time the contraction ring is examined to ascertain what,

if any, effect the present degree of anesthesia is having upon its tone. If a loop of cord is not present in the lower uterine segment, a painstaking cephalic application with midplane forceps is made. It may now be desirable, or even necessary, to deepen the anesthesia. Delivery is then effected by careful and steady traction, assisted by gentle pressure on the fundus in the direction of the pelvic inlet. If a loop of cord is present in the lower uterine segment, making it almost impossible for the cord to escape pressure from the forceps' blade,

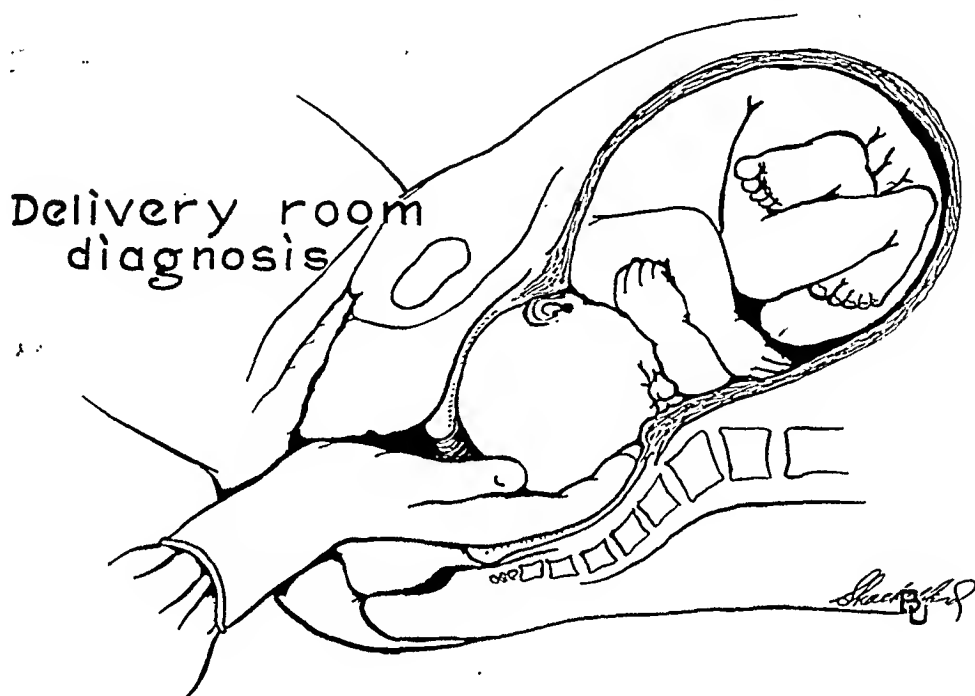


Fig. 7.—Under light anesthesia, hand is carried posteriorly between the fetal head and lower uterine segment to contact the ring. This is done to verify the diagnosis and to determine the method of delivery.

the writer prefers to lift the head up through the dilating or dilated ring, and complete the delivery by version and extraction. Adrenalin chloride will not dilate this type of ring. We tried it many times several years ago and always with the fingers trying gently to find a passage between the ring and the child's body. Ether and chloroform carried to the point of deep surgical anesthesia will relax it.

### Summary and Conclusions

1. The confusion in nomenclature and origin of contraction rings appearing in current textbooks is deplored.
2. It is assumed that those rings generally reported are of the severe variety and occur with obstructed labors.
3. Reasons are given for the firm conviction that a milder variety, or sub-clinical and larger group occurs with otherwise unobstructed labors.
4. Maternal mortality, operative incidence, and fetal mortality, as reported in a collective review of the literature, are compared with similar figures obtained from treatment of a large series of subclinical or early contraction rings.

5. The incidences of contraction rings in several institutions in Houston, Texas, are given to show the variance due to awareness of this complication of labor.

6. Early rupture of the membranes is believed to be a predisposing factor in the development of uterine rings.

7. Temporary or functional rings are recognized.

8. Cardinal signs and symptoms of ring dystocia are given, and the development and diagnosis of these rings are depicted in diagrams.

9. The usual methods of delivery in association with ring dystocia are described.

The author wishes to express his sincere appreciation to Miss Ella May Schakelford, medical artist, Baylor University College of Medicine, for the drawings.

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THE PERSISTENCE OF THE GONOCOCCUS IN THE FEMALE ADNEXA

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THE persistence of the gonococcus in the female adnexa over a prolonged period of time in patients who previously suffered from gonococcal infections is still a controversial subject.

A report of a study of operative gynecologic material obtained from 24 patients by Studdiford, Casper, and Scadron<sup>1</sup> showed that 66.6 per cent of such cases yielded positive gonococcus cultures, despite the fact that none of the patients was in the acute stage of the disease. On the other hand, Curtis<sup>2</sup> states: "It has almost never been possible to obtain gonococci in cultures from thoroughly ground Fallopian tubes removed from patients who have been free from fever and leucocytosis for a period of more than ten days or two weeks. The Fallopian tube appears, therefore, not to be a focus for chronic gonorrheal infection."

It must be emphasized that the above results were obtained in patients who had not received either sulfonamide or penicillin therapy. The object of this study was to determine whether or not such findings are still valid in the light of present therapy.

The operative material of 65 hospitalized female patients suffering from acute or chronic adnexal disease was examined bacteriologically for the presence of the gonococcus.

In order to ascertain the presence or absence of a gonococcal infection, an average of three urethral and cervical cultures was taken from each patient prior to operation.

A correlation of previous history of gonococcal infection and bacteriologic findings on admission is shown in Table I.

TABLE I. HISTORY AND BACTERIOLOGIC FINDINGS OF 65 CASES WITH PELVIC INFLAMMATORY DISEASE ON ADMISSION

PREVIOUS HISTORY OF GONOCOCCAL INFECTION	NUMBER OF PATIENTS	CULTURES			
		URETHRA		CERVIX	
		POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Denied	29		29		29
Admitted	22	10	12	20	2
Doubtful	14		14		14
Total	65				

The clinical diagnosis on admission is shown in Table II.

During hospitalization prior to operation, nine of the 45 women who had gonococcus negative urethral and cervical cultures received sulfonamide therapy.

TABLE II. CLINICAL DIAGNOSIS OF 65 PATIENTS ADMITTED TO THE GYNECOLOGICAL SERVICE AT BELLEVUE HOSPITAL

DIAGNOSIS	NO. OF PATIENTS
Chronic adnexal disease	26
Acute exacerbation of chronic adnexal disease	24
Pelvic abscess	3
Ruptured tuboovarian abscess	2
Fibromyoma and chronic pelvic inflammatory disease	7
Fibromyoma and chronic erosion of the cervix	1
Fibromyoma of the uterus	1
Degenerated fibroid	1
Total	65

Of the group of 20 gonococcus positive patients (in urethra and/or cervix), 10 became bacteriologically negative following sulfonamide therapy, two other patients were sulfonamide resistant, and two additional women responded to penicillin treatment prior to operation. The remaining six gonococcus positive cases (in urethra and cervix) received no treatment at all; nevertheless, two patients became spontaneously negative bacteriologically preoperatively. Consequently, there were only four untreated and two sulfonamide resistant patients who had gonococcus positive bacteriologic findings of the urethra or the cervix prior to their operation.

As a rule, no patient was operated upon before signs and symptoms of acute inflammation had subsided and the sedimentation rate had become normal.

Immediately following operation the majority of the patients received sulfonamide therapy or penicillin treatment in order to prevent possible complications of the infection. No spread of the infection occurred among these patients.

#### Method Used for the Bacteriologic Examination of Operative Material

The bacteriologic technique employed in examining the operative material was as follows: Culture material was taken from any exudate present in the abdominal cavity, particularly from the surface of the uterus or adnexa. By compressing the fimbriated end of the inflamed Fallopian tubes, it was occasionally possible to obtain culture material before surgical removal. As soon as the uterus or the adnexa or both had been removed, these organs were opened under sterile precautions. Culture material was taken as follows: (1) from the surface of the mucous membranes, (2) from the deeper layers by scraping the mucosa with a sterile knife, and (3) by dissecting pieces of tissue from the various layers of the organs. The culture material was collected with the aid of sterile swabs and then immersed into separate tubes containing 2 per cent peptone water.

The tubes containing the culture material were taken to the laboratory and cultured within two hours. Two plates were inoculated: one onto Peizer medium<sup>3</sup> and the other onto a medium<sup>4</sup> which has been proved to be equally good at our laboratory. Larger pieces of the operative tissue were further ground up into smaller particles and transferred onto the two different culture media. All the inoculated plates were incubated for the first twenty-four hours under 10 per cent carbon dioxide tension at 37° C., and for another twenty-four hours at the same temperature without carbon dioxide. The plates were

\*This medium consists of 500 c.c. of Difco Bacto Proteose III Agar, 25 c.c. of citrated hemolyzed horse blood, 40 c.c. of ascitic fluid.

then read, and any suspicious gonococcus colonies were identified by smears, fermentation tests, lack of growth on plain agar, and absence of hemolysis on 5 per cent horse blood agar plates.<sup>4</sup>

### Bacteriologic Findings of the Operative Material

The bacteriologic findings of the operative material of the 65 patients are as follows:

1. No gonococci were found in the operative material obtained from the 45 women whose cervical or urethral secretions were found to be gonococcus negative preoperatively.

2. No gonococci were found in the operative material of the 12 women whose cervical and urethral discharges were initially gonococcus positive, but who responded to sulfonamide or penicillin treatment prior to operation.

3. Gonococci were found in the operative material of only four of the eight initially gonococcus positive patients who received no treatment or did not respond to sulfonamide therapy prior to operation. Of these four patients whose operative material showed the presence of the gonococcus, three had not received any treatment, and one was resistant to sulfonamide therapy (Table III).

### Comment

In our series the bacteriologic findings of operative material indicate that gonococci persisted in the female adnexa only in four of the eight untreated or treatment-resistant patients. In addition, negative bacteriologic findings in the operative material were obtained from 12 originally infected patients who were adequately treated preoperatively. These findings suggest the value of administration of adequate amounts of penicillin to patients with pelvic inflammatory disease prior to operation, particularly to those patients who have an antecedent history of gonococcal infection. This course as a routine procedure may diminish the danger of postoperative complications.

It is also noteworthy that somewhat more than 33 per cent of the operative material yielded no growth of any organism whatever on the special media used, despite the presence of an acute or chronic inflammatory process.

### Illustrative Cases

The following two cases illustrate the histories and pre- and postoperative bacteriologic and pathologic findings of a gonococcus positive and a gonococcus negative case.

CASE 1.—C. L., a 20-year-old single Puerto Rican girl had repeated gonococcal infections. She was treated for gonorrhea with sulfonamides in Harlem Hospital in 1941. According to her history, ankle and toe joints were also affected at that time. She was admitted to Bellevue Hospital in 1943 for pelvic inflammatory disease and vaginal discharge. In March, 1944, she was treated with sulfathiazole in Bellevue Hospital because of gonococcal urethritis, cervicitis, and salpingitis. She was again admitted to Bellevue Hospital on Oct. 19, 1944, because of bilateral abdominal pain of twelve hours' duration, and a temperature of 100.2° F.

*Examination.*—There was tenderness and spasm on both lower quadrants. The cervix was posterior and firm. The uterus was of normal size, anterior, and tender on motion. There was a bilateral tender adnexal mass, 4 cm. in diameter. The cervix showed a cervicitis with bleeding erosion.

*Diagnosis.*—Acute exacerbation of chronic salpingitis, right and left tubo-ovarian abscesses.



TABLE III. BACTERIOLOGIC FINDINGS OF OPERATIVE GYNECOLOGIC MATERIAL REMOVED FROM EIGHT INFECTED, UNTREATED, OR TREATMENT-RESISTANT PATIENTS

CASE	DIAGNOSIS	BACTERIOLOGIC FINDINGS ON ADMISSION		THERAPY	RESULT OF THERAPY	DURATION OF PELVIC INFLAMMATORY DISEASE PRIOR TO ADMISSION	BACTERIOLOGIC FINDINGS PRIOR TO OPERATION		INTERVAL BETWEEN POSITIVE FINDINGS AND OPERATION (DAYS)	BACTERIOLOGY OF OPERATIVE MATERIAL			
		URE-THRA	CER-VIX				URE-THRA	CER-VIX		UTERINE CAVITY	RIGHT FALLOPIAN TUBE	RIGHT OVARY	LEFT FALLOPIAN TUBE
1	Chronic adnexal disease, or ectopic pregnancy	Neg.	Pos.	None	—	About 5 weeks	Neg.	Pos.	7	—	Sterile	—	—
2	Acute exacerbation of chronic salpingitis	Neg.	Pos.	None	—	About 6 weeks	Spontaneous negative		34	—	—	Neg.	—
3	Acute exacerbation of chronic adnexal disease	Pos.	Pos.	None	—	Similar attack 3 years ago, acute exacerbation for 4 days	Spontaneous negative		32	—	—	Neg.	Neg.
4	Acute exacerbation of chronic salpingitis, right and left tuboovarian abscess	Pos.	Pos.	Sulfathiazole 12 Gm.	Resistant	1943, pelvic inflammatory disease—March, 1944, gonococcal salpingitis, acute salpingitis one day	Pos.	Pos.	11	—	Pos.	Pos.	—
5	Pelvic inflammatory disease	Pos.	Pos.	None	—	About 5 months	—	Pos.	4	Pos.	Sterile	—	—
6	Acute exacerbation of chronic adnexitis	Pos.	Pos.	Sulfathiazole 12 Gm.	Resistant	Repeated attacks for 7 years, acute exacerbation for 2 days	Pos.	Pos.	3	—	Sterile	Sterile	—
7	Pelvic inflammatory disease, bilateral pyosalpinx, tuboovarian abscess	Neg.	Pos.	None	—	Gonorrhea 3 months ago	Neg.	Pos.	57	—	Pos.	Neg.	Neg.
8	Endoecervicitis, subacute salpingitis, tuboovarian abscess	Pos.	Pos.	None	—	Episodes of adnexal inflammations for 7 years	Pos.	Pos.	16	—	Pos.	Pos.	Pos.

Positive = gonococcus present. Negative = gonococcus absent. — = no examination performed.

*Therapy.*—The patient received 12 Gm. of sulfathiazole, but remained positive on urethral and cervical cultures.

*Operation.*—Laparotomy was performed on Oct. 28, 1944, eleven days after the last gonococcus positive findings.

*Findings.*—The uterus was anterior and normal in size. The left tube was normal in size but tortuous and extruding pus from the fimbriated end. The right tube was enlarged to four to five times the normal size and was filled with pus. The ovary was enlarged three to four times the normal size, cystic, and adherent with the tube to the posterior aspect of the broad ligament. There were many adhesions of the intestines to the adnexa.

*Operative Procedure.*—A right salpingo-oophorectomy and a left salpingectomy was done. Five grams of sulfathiazole were sprinkled into the abdominal cavity.

*Postoperative Course.*—The postoperative course was essentially uneventful from the surgical point of view. The patient was given 100,000 Oxford units of penicillin, because here cultures taken on the sixth postoperative day were still gonococcus positive.

*Laboratory Findings.*—

*Preoperative:* Urethral and cervical cultures were gonococcus positive on October 11 and October 18.

*Operative material:* The cultures from the operative material from the right tubal abscess, right tube, right ovary, and left tube were positive for the gonococcus. One of the positive cultures from the left tube was obtained by squeezing out the tube before its removal.

*Postoperative:* Cultures taken on the sixth day after the operation were still positive for the gonococcus. After the patient was given 100,000 Oxford units of penicillin, her cultures became negative.

*Pathologic Diagnosis.*—Bilateral pyosalpinx with subacute follicular salpingitis, corpus luteum hematoma, and peritoneal adhesions.

*Discharge.*—The patient was discharged on the twenty-first day after the operation.

CASE 2.—E. B. (Hospital No. 28013-44), a 41-year-old white married woman with no history of previous gonococcal infection was admitted to Bellevue Hospital on June 18, 1944, because of abdominal pain in both lower quadrants of ten days' duration. She had been married for seventeen years, and had had three miscarriages in the first three years of her married life. In 1928, sixteen years ago, the patient was admitted to Roosevelt Hospital because of abdominal pain and fever; a pelvic abscess was opened by posterior colpotomy. In March, 1944, she had a similar attack of right lower abdominal pain with vaginal bleedings, lasting for about ten days; the condition improved after bed rest. For the last five years she suffered from diabetes mellitus.

*Examination.*—On admission there was tenderness and an increased resistance in the right lower abdominal quadrant. The cervix was anterior, closed, and firm. The fundus uteri could not be felt. There was a 12 cm. tender, cystic mass, filling most of the pelvis, extending deep into the cul-de-sac, and rising up to two fingers above the symphysis.

*Diagnosis.*—Right tuboovarian abscess, diabetes mellitus.

*Therapy.*—No sulfonamide or penicillin therapy was given.

*Operation.*—Laparotomy was performed on Aug. 14, 1944, fifty-six days after admission and after gonococcus negative findings.

*Findings.*—The uterus was anterior, normal in size. The ovaries were densely adherent to the posterior aspect of the broad ligament. Otherwise they were normal except for fibrosis. The left tube was thickened to twice the normal size, with a sealed ampulla and adherent to the broad ligament. The outer third of the right tube formed a 6 cm. cystic mass, filled with pus.



*Operative Procedure.*—A supraeervical hysterectomy and bilateral salpingo-oophorectomy was done.

*Postoperative Course.*—The postoperative course was uneventful.

*Laboratory Findings.*—

*Preoperative:* Urethral and cervical cultures were negative.

*Operative material:* Five cultures from both tubes and ovaries of the operative material were gonococcus negative.

*Pathologic Diagnosis.*—Proliferation of endometrium uteri. Bilateral subacute salpingitis with pyosalpinx. Right cystic hydatid of Morgagni. Unclassified cysts of right ovary. Peritoneal adhesions.

*Discharge.*—The patient was discharged on the twenty-seventh postoperative day.

### Summary and Conclusions

1. Operative material from 65 hospitalized female patients suffering from acute and chronic adnexal disease was examined bacteriologically for the presence of the gonococcus.

2. Forty-five women with adnexal disease had persistent gonococcus negative bacteriologic findings, both pre- and postoperatively, and also in their operative material.

3. The remaining 20 cases were gonococcus positive preoperatively. Twelve of these were successfully treated preoperatively and showed gonococcus negative bacteriologic findings in their operative material.

4. Of the remaining eight patients, two became gonococcus negative spontaneously, and yielded negative bacteriologic findings on their operative material.

5. Of the remaining six, two patients were resistant to sulfonamide therapy, the operative material of one of these cases was gonococcus positive. Of the remaining four cases, all of which were positive preoperatively, only three yielded positive bacteriologic findings.

6. All cases which were successfully treated for their gonococcal infection proved to have gonococcus negative bacteriologic findings in their operative material.

7. The bacteriologic findings of this study indicate that the persistence of the gonococcus in the female adnexa is limited to untreated or treatment-resistant patients.

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# INTRAPARTUM FEVER: A PRELIMINARY STUDY

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IN RECENT years the clinical importance of intrapartum fever has not received the attention it deserves. Except for older European studies<sup>1-10, 13-16, 18, 20</sup> little effort has been made to investigate this serious complication of parturition. Previous observations have demonstrated that the appearance of fever during labor alters considerably the maternal and fetal prognosis (Table I).

TABLE I. INTRAPARTUM FEVER: REVIEW OF LITERATURE

AUTHOR	YEAR	TOTAL NUMBER OF DELIV- ERIES	TOTAL NUMBER OF INTRA- PARTUM FEVERS	INCI- DENCE OF INTRA- PARTUM FEVERS (%)	MA- TERNAL MORBID- ITY (38°+) (%)	MA- TERNAL MORTAL- ITY (%)	INFANT MORTAL- ITY (%)	OPER- ATIVE INCI- DENCE (%)
Odell and Plass	1926-1942	15,826	187	1.1	42.8	8.0	36.9	42.2
Anderson	1937	11,075	207	1.9	63.8	7.7	33.4	48.8
Hilgenburg	1931	3,558	150	4.2	54.0	4.0		50.0
Matere	1930		61		52.2	9.8	41.0	61.1
Siebert	1928		87		48.63			
Lankovitz	1924-1928	22,127	290	1.3	30.0	1.0	32.8	(low)
Zangemeister	1915-1927	14,499	538	3.7	49.0	7.6	35.0	49.8
Zangemeister*	1925-1927		100		41.0	0	33.5	50.0
Henkel	1913-1921	3,240	117	3.6	38.0	3.4	29.9	38.3
Warnekros	1913		151			4.0		
Ihm	1897-1903	7,554	200	2.7	41.5	4.0		50.0
Ahlfeld	1893	3,000	62		65.5	6.2		49.0
Glockner	1891	1,000	211	21.1	32.7	7.1	35.5	
Winter†			53	62.0	8.0	35.0		
Wichman†			110	14.0	7.0			
Rhode†		4,279	90	2.1				
Liepmann†		1,212	126	10.4				
Kronig†				2.9				

Values in the various percentage columns should not be subjected to direct comparison because of the different criteria employed in compiling the data.

\*Second series of cases.

†From Zangemeister and Welck.<sup>1</sup>

According to most authors<sup>1-11, 13, 15, 16, 19, 20</sup> the diagnosis of intrapartum fever is established if the temperature reaches 100.4° F. (38° C.). Confusion over etiology and proper treatment has led to a diversity in therapy. Both operative and conservative managements have been recommended. The present study was made to investigate our experience with febrile labors and to suggest acceptable treatment.

## Material

In the period July 1, 1926, to July 1, 1942, at the University Hospitals, there were 187 labors attended with fever.\* Only those patients giving birth to children weighing over 1,500 grams have been included. Patients with afebrile uterine infections† have not been considered.

\*100.4° F. or 38° C.

†Putrid amniotic fluid without fever.

### Incidence

The incidence of intrapartum fever was 1.2 per cent, 1 in 85 deliveries. The higher incidence in previous reports (Table I) is best explained by (a) inadequate obstetric techniques and lack of prenatal care in the late nineteenth and early twentieth centuries,<sup>2, 3, 4, 10, 16</sup> (b) the inclusion of the influenza epidemic of 1918 to 1919,<sup>1, 15</sup> (c) the inclusion of patients with afebrile genital infections,<sup>1</sup> and (d) the use of 35 cm. instead of 1,500 Gm. as the dividing line between late abortion and premature labor.<sup>1-11, 13-16, 19, 20</sup> The incidence of intrapartum fever in most modern clinics probably lies between 1 and 2 per cent.

### Etiology

Intrapartum fever may be due to metabolic, extragenital, or genital causes (Table II). Dehydration fever has long been a recognized clinical entity. Pride, et al.<sup>21, 22</sup> have demonstrated ketosis (ketone bodies in urine) and lower CO<sub>2</sub> combining power in prolonged labors. Vomiting and reduced caloric intake commonly lead to the development of ketosis. A steadily decreasing CO<sub>2</sub> combining power may be evidence of lactic acid accumulation within the tissues.<sup>21, 22</sup> The older idea<sup>2, 3</sup> that fever in prolonged labor may be due to muscular exertion and thus be comparable to that detected in long distance runners is not inconsistent. Intrapartum fever due to dehydration (inanition) develops late in labor. The temperature seldom rises above 102° F., and falls after the administration of fluids and dextrose. Toxic symptoms (chills, malaise, etc.) and evidence of genital or extragenital infection are absent. If the patient's temperature is taken frequently during labor these asymptomatic fevers will not be overlooked.

Several extragenital sources of intrapartum fever have been reported. The pyrexia in eclampsia is generally considered central in origin.<sup>23</sup> However, placental infection<sup>17, 18</sup> has been described in eclamptic patients, particularly when labor has been surgically induced. Intrapartum fevers due to respiratory, urinary, and contagious diseases may occur (Table II).

Warnekros,<sup>6, 7</sup> Slemons,<sup>11, 12</sup> and Siddall<sup>26</sup> demonstrated bacteria within the amnion, subamnion, and intervillous spaces. Seventy per cent of positive maternal blood cultures were reported in patients with intrapartum genital infections.<sup>6, 7</sup> Although later investigation<sup>1</sup> failed to confirm such a high rate of bacteremia, it is obvious that, in the presence of placentitis, the maternal and fetal circulations can easily be invaded from the adjacent intervillous spaces. Depending upon various factors (type and virulence of the organisms, resistance of the host, and adequacy of cervical drainage) amnionitis may or may not produce a febrile response and foul-smelling amniotic fluid. In the absence of fever, there may be some doubt concerning the pathogenic character of the invaders. Fever, when present, is commonly accompanied by chills, malaise, and other toxic manifestations. Uterine inertia is usually present.

Rarely, the uterus may be tender and tense from gas accumulation; percussion over the fundus may elicit tympany ("balloon" sound<sup>1</sup>). Genital infections may occur in combination with dehydration and other extragenital sources of fever (Table II).

TABLE II. THE RELATION OF THE ASSIGNED CAUSE OF THE PYREXIA TO MATERNAL AND FETAL COMPLICATIONS

	DEHYDRATION		EXTRAGENITAL SOURCE		GENITAL INFECTION		COMBINED CAUSES	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Total	39	20.8	19	10.2	66	35.3	63	33.7
Maternal deaths	0	0.0	7	36.8	5	7.5	3	4.7
Child, death	0	0.0	8	42.2	28	42.4	33	52.4
Child, asphyxia	6	17.9	2	10.5	29	43.9	32	50.8
Child, infection	3	7.7	1	5.3	6	9.0	8	12.7
Febrile puerperium	1	2.5	11	57.9	35	53.1	39	61.9
Maximum intra-partum fever—								
100.4-101	25	64.2	5	26.3	23	34.8	18	28.6
100.1-102	13	33.3	7	36.8	26	39.4	22	34.9
Over 102	1	2.5	7	36.8	17	25.8	23	36.5

"Combined causes" represent those cases with genital infections plus one or more extragenital sources of fever. "Extragenital sources" include eclampsia, ten; urinary tract infection, four; pneumonia, three; infectious diarrhea, one; and measles, one.

There are several other factors associated with the development of intrapartum fever. As high as 50 per cent of intrapartum fevers have been reported<sup>13</sup> as occurring in patients with prematurely ruptured membranes.\* Prolonged labor (over thirty hours' duration) has been similarly associated with fever,<sup>27</sup> probably the result of dehydration and numerous rectal (or vaginal) examinations.† The effects of pre-existing genital infection (condylomas, Bartholinitis), poor pregnancy hygiene, and excessive vaginal manipulation<sup>20</sup> are self-evident. The high percentage of toxemic patients in this series may be related to necessary induction of labor (artificial rupture of the membranes or bag induction).

### Maternal Morbidity

A high postpartum morbidity rate is to be expected in patients with intrapartum fever, particularly of genital origin. Operative delivery is often deemed necessary because of uterine inertia; and the pre-existing infection, as well as the trauma of operation, contributes to the development of puerperal sepsis. Patients with eclampsia, and with fevers of respiratory and urinary tract origin are likewise prone to develop puerperal infections, although those with dehydration fever are usually free from sequelae (Table II). Eighty women (45.9 per cent) in this series were febrile after delivery, and 35 had relatively serious puerperal complications‡ (Table III). The bacteriologic findings were di-

\*In this series 47.6 per cent had prematurely ruptured membranes.

†In this series 73 patients (41 per cent) had prolonged labors.

‡Parametritis, fifteen; pneumonia, eleven; peritonitis, four; septicemia, four; and thrombophlebitis, one.

TABLE III. FEBRILE PUERPERAL COMPLICATIONS

	PATIENTS	
	NUMBER	PER CENT
Endometritis*	70	37.4
One-day fever	28	14.9
Parametritis	15	8.0
Pneumonia	11	5.8
Pyelitis	10	5.2
Peritonitis	4	2.1
Septicemia	4	2.1
Thrombophlebitis	1	0.5

\*Fever lasting more than one day and not associated with a demonstrable extragenital cause of fever or with evidence of pelvic infection outside the uterus. Diagnosis made by exclusion.

The total of these percentages is greater than the reported incidence of febrile puerperium because some patients fell into more than one category.

TABLE IV. MATERNAL BACTERIOLOGIC FINDINGS

ORGANISM	CERVICAL CULTURE	URINE CULTURE	BLOOD CULTURE
Total	26	14	24
No growth	0	0	20
E. coli	5	11	0
Gonococcus	4	0	0
Staphylococcus aureus	1	1	1
Diphtheroid	2	0	0
Staphylococcus albus	7	1	0
B. hemolytic streptococcus	5	0	3
Alpha hemolytic streptococcus	7	0	0
Nonhemolytic streptococcus	3	0	0
Anaerobic hemolytic streptococcus	2	0	0
Bacteria pyocyanase	1	1	0

Death occurred in all patients with positive blood culture. Cervical cultures occasionally revealed more than one organism.

versified but death occurred in all patients with positive blood cultures (Table IV).

### Maternal Mortality

The gross maternal mortality rate was 8.0 per cent (15 patients), but eclampsia<sup>3</sup> and extragenital lesions (pneumonia, two; and arsenical encephalitis, two) contributed almost one-half. (See case reports for review of all maternal deaths.) According to the standards of the Division of Maternal Welfare of The Bureau of Vital Statistics, the maternal deaths would be classified as follows:

Nonobstetric deaths	4
Albuminuria and eclampsia	3
Shock and accidents of labor	3
Puerperal sepsis	3
Hemorrhage	1
Thrombophlebitis and embolus	1

Intrapartum fever in a patient with eclampsia or severe respiratory infection is often followed by postpartum shock, pneumonia, sepsis, and death. In this series postpartum shock was observed in five patients, of whom four expired. The specter of death is constantly before those with febrile labors of genital origin, particularly if difficult operative delivery is necessary.

### Infant Mortality and Asphyxia

*High stillbirth and neonatal death rates have been constant findings in women with intrapartum fevers (Table I). Prematurity is responsible for some*

deaths (Table V) but infected amniotic fluid also unfavorably alters the prognosis for the infant. Fetal pneumonia<sup>24</sup> from aspiration of the infected fluid has been described; the pneumonic process is frequently limited. According to Potter<sup>24</sup>:

"Pneumonia may be present in stillborn or liveborn infants. It is rarely either distinctly bronchial or lobar in distribution but usually entails diffuse involvement of irregularly scattered alveoli. It is of intrauterine origin since squamous cells from inspired amniotic fluid are frequently associated with the polymorphonuclear leukocytes in the alveoli. Little or no fibrin is present and areas of hemorrhage of the lungs, especially when these occur in partially atelectatic areas, may produce the same appearance. Sections of the lungs should be examined microscopically in all cases in which pneumonia is suspected, before a positive diagnosis is made. In fact, a positive statement as to the presence or absence of pneumonia in a stillborn or a newly born infant can rarely be made except on microscopic examination."

TABLE V. SUMMARY OF AUTOPSY FINDINGS IN 48 INFANTS\*

	ANTEPARTUM DEATHS INFANTS		INTRAPARTUM DEATHS INFANTS		NEONATAL DEATHS INFANTS	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Total (autopsied)	6		31		11	
Prematurity	3	50.0	6	19.7	1	9.0
Maceration	4	66.6	5	16.2	0	0.0
No significant lesion	2	33.3	9	29.1	1	9.0
Septicemia	0	0.0	1	3.2	1	9.0
Subcutaneous abscess	0	0.0	0	0.0	1	9.0
Intracranial hemorrhage						
Slight	0	0.0	5	16.6	0	0.0
Severe	0	0.0	7	23.3	7	63.6
Marked atelectasis	6	100.0	31	100.0	0	0.0
Miscellaneous	3	50.0	0	30.0	1	9.0
Total available lung sections reviewed by E. Potter	2		24		10	
Fetal pneumonia	1	50.0	12	50.0	6	60.0

\*There were many multiple diagnoses.

Among 19 cases with evidence of fetal pneumonia (E. Potter), eight had been previously described by other pathologists as showing no significant lesions. The miscellaneous group included fetal asphyxia, two; intra-abdominal hemorrhage, four; hydrocephalus, one; meningomyelocle, one; anencephalus, two; erythroblastosis fetalis, one; congenital lues, one; and extensive hemorrhage into the neck, one.

The histologic sections available in this series were reviewed by Potter, who found pneumonia in 50 per cent of the stillborn and in 60 per cent of the neonatally dead infants (Table V). Other investigations<sup>6, 7, 11, 12</sup> suggest placental invasion and subsequent fetal septicemia as the chief cause of death. The lack of significant findings in some autopsied infants is puzzling (Table V). Fulminating fetal septicemia may cause death so quickly that there is insufficient time for anatomic changes to develop. On the other hand, the bacterial invasion of the blood may represent merely a harmless bacteremia. The fetus must depend upon the mother for immunologic protection. If maternal defenses are inadequate the fetus has little chance to escape a blood stream infection.

Recently, two patients developed intrapartum fever with signs of genital infection. The first was spontaneously delivered of a stillborn infant, the culture of whose heart blood disclosed alpha hemolytic streptococci. The same or-



ganism was recovered from the child's lung, the placenta, and the mother's cervix. Microscopic examination of the lung revealed no pneumonic process. The second patient was delivered of a living infant after Dührssen's incisions by midforceps extraction because of uterine inertia. Blood culture from the infant (fontanel puncture) disclosed hemolytic staphylococcus aureus, the organism being recovered from the infant's groin and the mother's cervix. In spite of the bad prognosis of a staphylococcus septicemia, the prompt administration of sulfathiazole (commenced immediately after birth in anticipation of such a complication) was followed by complete recovery.

Whether aspiration pneumonia and septicemia from placental invasion are independent or dual causes of fetal (or neonatal) death in genital infections of the parturient will be the primary objective of future investigation. In eclampsia the high infant mortality rate has been attributed to prematurity and anoxia from hypnotic drugs,<sup>23</sup> or to traumatic delivery resulting in severe intraeranian damage (Table V). While evaluation of the effect of the ma-

TABLE VI. FACTORS AFFECTING CHILD DEATH RATES

	TOTALS	ANTEPARTUM DEATHS INFANTS		INTRAPARTUM DEATHS INFANTS		NEONATAL DEATHS INFANTS	
		NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Child deaths	69	10	14.5	41	59.4	18	26.1
Operative delivery	75	5	6.6	25	33.3	9	12.0
Height of intra-partum fever—							
100.4°-101° F.	73	3	4.1	10	13.7	4	5.4
101.1°-102° F.	67	1	1.5	13	19.4	6	8.9
Over 102° F.	47	6	12.8	18	38.3	8	17.0
Prematurity (under 2,500 grams)	38	4	10.5	9	23.6	4	10.5

The height of the intrapartum fever (possibly a measure of the virulence of the infecting organisms) correlated directly with the fetal and neonatal death rates.

ternal pyrexia is problematic, the height of fever during labor, a measure of bacterial virulence, and the resistance of the organism, shows a direct relationship with the fetal death rate. This suggests infection as an important cause of death (Table VI).

Asphyxia is frequently encountered in infants delivered from febrile parturients. Genital infection, prolonged labor, and operative delivery were the most significant factors influencing the incidence of asphyxiation. Asphyxia neonatorum (of some degree) was encountered in 121 infants (64.7 per cent). It has been suggested that toxins transmitted through the placenta or absorbed from the respiratory tract may be important causes of fetal asphyxia during febrile labors. On the other hand, fetal asphyxia is frequently the result of intraeranian injury in children subjected to prolonged or operative deliveries.

### Therapeutic Considerations

Any approach to the treatment of intrapartum fever must include both diagnostic and therapeutic aims. Early diagnosis of the cause of fever during labor alters prognosis and management. In general, the necessary diagnostic procedures are relatively simple. Urinalysis will detect evidence of urinary tract infection and of ketosis. Physical examination will reveal upper respira-

tory infection or exanthemas. The uterus should be carefully palpated for tenderness, consistency, and tympany. A foul odor about the genitals suggests infected amniotic fluid even before expulsion of the child. Adequate bacteriologic investigation (cervical, throat, urine, and blood cultures) is important, especially in patients exhibiting chills, high fever, and toxicity.

The administration of intravenous fluid, especially dextrose solution, is recommended for its general effect and to evaluate the role of dehydration in the development of the fever. Pride, et al.<sup>21, 22</sup> recommend 4.0 Gm. of sodium bicarbonate by mouth in prolonged labors in the belief that postpartum shock may be prevented by reducing the acidosis. Except in severe respiratory infections, adequate sedation with morphine is indicated to conserve maternal strength. Chemotherapy with penicillin or sulfonamides is of definite value in serious infections. The maternal morbidity and infant mortality rates incident to febrile labors can be reduced by intramuscular penicillin or by intravenous sodium sulfathiazole before delivery. To test the efficacy of administering sulfonamides during labor, two mothers with uncomplicated labors were given 5.0 Gm. of sodium sulfathiazole intravenously two hours forty-six minutes, and three hours twenty-five minutes before delivery. The respective blood sulfathiazole levels of the mother and child at the time of delivery were 7.8 mg. per 100 c.c., of blood and 6.0 mg. per 100 c.c. in the first case, and 5.8 mg. per 100 c.c. of blood and 6.0 mg. per 100 c.c. in the second case.

TABLE VII. INDIVIDUAL BACTERIOLOGIC FINDINGS

NAME	BLOOD CULTURE	MOTHER CERVICAL CULTURE	INFANT BLOOD CULTURE	PLACENTAL CULTURE	AUTOPSY FINDINGS
D. G.	No growth	Beta hemol. strep. (Lancefield B)	Beta hemol. strep. (Lancefield B)	Not done	No significant finding
R. C.	No growth	Alpha hemol. strep.	Alpha hemol. strep.	Alpha hemol. strep.	†No significant finding
M. L.	No growth	Staph. aureus, alpha hemol. strep.	Staph. aureus, alpha hemol. strep.	*Overgrown	No significant finding
R. B.	No growth	Staph. albus	Hemol. staph. aureus	Not done	Discharged alive
K. J.	No growth	Alpha hemol. strep. and hemol. staph. aureus	No growth	E. coli	Discharged alive

\*The culture was overgrown with pseudomonas pyocyanea often inhibitory to the growth of pathogens.

†No significant anatomic lesion other than atelectasis was found at autopsy.

Note the similarity of the bacterial flora from fetal blood, maternal cervix and placenta.

It is dubious if intrapartum fever constitutes an acceptable indication for operative delivery, and previous investigations<sup>1, 14, 19, 20</sup> have consistently stressed this doubt. With the exception of older reports, a high operative incidence was uniformly associated with high maternal mortality and morbidity rates (Table I). Although operative intervention may save some infants, the accoucheur hesitates to subject infected maternal tissues to traumatic procedures in face of the probability that future pregnancies will be safely com-

with deep appreciation, our debt to these two teaching centers for having made this most practical instruction available to our physicians.

In 1940, we had reached a maternal mortality rate of 17 per 10,000 live births, and we felt that some improvement had been made. Then the rate began to rise. It was 26 per 10,000 live births in 1941, 25 in 1942, 29 in 1943. In 1944 it had fallen to 18, and the provisional rate for 1945 is 11 per 10,000 live births. Statistically, this rise and fall within rather narrow limits does not seem important to me. But it did not seem important that our rate of 29 per 10,000 live births in 1943 coincided with the year in which deaths from obstetric hemorrhage went into first place, ahead of infection and toxemia. An analysis of the individual case summaries of maternal deaths from hemorrhage during that year showed that two factors were chiefly responsible for the rise: (1) injudicious operative obstetrics, and (2) inadequate blood substitutes.

The first factor is not limited to North Dakota! It is nationwide. It first began when panic seized the first obstetrician in the presence of dystocia, it increased under the false assumption that modern operating rooms had made cesarean section the best way out of obstetric difficulties, and it was further encouraged by the false sense of security provided by sulfonamide therapy and, later, penicillin. The end is not yet. Intensive education is still needed to impress present and future medical generations with its dangers.

The second factor, inadequate blood substitutes, was a particularly important one in North Dakota. I read several case histories of deaths from hemorrhage, ascribed to placenta previa. In four of these cases in one year and in widely scattered areas, blood donors had, eventually, been obtained; but not before the irreversible reaction had set in. In Grand Forks we had been working on a pooled liquid plasma project. One of my partners, Doctor R. O. Goehl, and the Director of the Division of Laboratories of the State Health Department, Mr. Melvin E. Koons, had shown the safety of this product for local use. The product they prepared was highly satisfactory when kept under proper storage conditions, but we soon came to the conclusion that it would not be practical or safe for statewide distribution.

Mr. Koons set to work to see if we could manufacture dried human plasma, and we set out to get a bill through a special session of the North Dakota Legislature in February, 1944, authorizing the establishment of a State Plasma Bank in the Public Health Laboratory at the University of North Dakota. Both projects were successful, and an initial appropriation of \$10,000.00 was granted. The University of North Dakota added additional funds and supplied the space necessary for the plasma bank. The first dried human plasma had passed its tests by August 27, 1944. It seemed interesting to have data available to show the results of the first year of operation. I am indebted to Mr. Koons for the tables:

Thus, it will be seen that about 18 per cent of the patients who received North Dakota-made plasma during the first year of operation of the plasma bank were obstetric patients.

pediatric seminars at six convenient centers. Highlighting these all-day seminars were the round table discussions that featured each. The committee obtained splendid cooperation from the officers of the various medical societies in making local arrangements for them and in advertising them to their members. We continued this type of instruction through 1938. A recent questionnaire regarding them resulted in a request from a majority of our physicians that they be renewed.

In 1937, we asked the Maternal and Child Hygiene Division and the Division of Vital Statistics of the State Health Department to begin an analysis of each maternal death that occurred in North Dakota. Only two stipulations were made by the committee: The name of the attending physician and the place of death of the patient were to remain anonymous as far as the data, submitted to the committee, were concerned. Trained physician investigators from the State Health Department have conducted these investigations, and they have had the full cooperation of the medical profession. From an analysis of the yearly surveys, the committee has been able to discover certain trends and recommend certain corrective measures which we feel have been of benefit to the physicians and their obstetric patients. Two items only will be mentioned. The committee recommended a uniform summary record for all hospitals admitting maternity patients. This record is now in use throughout the state. We recommended consultation before all cesarean sections. This consultation rule is being adopted.

In 1938 the Maternal and Child Welfare Committee sponsored the founding of the North Dakota Society of Obstetrics and Gynecology. It began with nine members and now has 36, seven of whom are diplomates of the American Board of Obstetrics and Gynecology, three more limit their practices to those specialties, and 26 are general practitioners. We cannot be accused of specialist domination! The Society has flourished since its inception. It has had excellent program meetings and has always worked hand in hand with the State Medical Association.

In 1938, I suggested to the Maternal and Child Welfare Committee that postgraduate education for North Dakota physicians be broadened to include short courses in residence at near-by teaching centers. This proposal had the enthusiastic support of Doctor William A. O'Brien, Director of the Center for Continuation Study at the University of Minnesota, and the North Dakota State Health Department furnished the stipends for ten North Dakota physicians to attend the first course. The physicians were selected by application through their district medical societies. There were sixty applicants for the ten places. The first course was given at the University of Minnesota in May, 1939. The plan was continued and enlarged. Through the splendid cooperation of Doctor Everett D. Plass, the Department of Obstetrics and Gynecology of the University of Iowa agreed to take our physicians for their bedside teaching course in obstetrics. To date, over 150 North Dakota physicians of the 360 in the state have availed themselves of postgraduate instruction in these courses at the University of Minnesota and the University of Iowa, and the requests for this type of instruction have not diminished. We acknowledge,

tice in North Dakota by bringing them into close teaching contact with a number of the excellent practitioners throughout the state. In this way we feel that our medical students and young graduates would come to love North Dakota, even as I have come to love it, by intimate contact with its people. This is not a program for a day or for a year, but it is a long-range program that will have both tears and triumphs along its way.

We have come far enough along the way in medical education in North Dakota to know that in obstetrics, for example, our physicians are eager for the best. They want postgraduate education made more readily available to them and this a Center, such as I have indicated, can provide. I have seen how well the all-too-few opportunities that have been provided for postgraduate instruction in obstetrics have been utilized in the saving of the lives of mothers. We have only begun.

### Discussion

DR. GEORGE W. KOSMAK, New York, N. Y.—Dr. Moore's contribution exemplifies the progress in obstetrics in his locality through the medium of individual efforts by conscientious and enthusiastic practitioners, by efforts stimulated from within and not from without. The presentation discloses, moreover, that simplicity of procedure may be equally effective in producing results as the more elaborate and costly methods by which the graduates of our medical schools and many of our hospitals have become infected. It should still be possible to conduct satisfactory deliveries under ordinary circumstances even in the homes, in areas where hospital facilities are not readily available, or where poor hospitals constitute a danger in themselves.

Naturally enough, Dr. Moore stresses the desirability of hospital deliveries, but, with proper preparation, a home delivery can be made almost equally satisfactory, if perhaps less convenient for the physician. Of course it is a matter of environment, and the environment must be made safe. That depends on the doctor, and the nurse, and the family. Perhaps we can never reach that stage of perfection when there will be provided universal, adequate, and competent hospital care, and in the meanwhile we may have to improvise. There may be areas where medical facilities are inadequate, but there is still an aid in the properly supervised trained nurse-midwife, to whom, however, Dr. Moore does not refer.

Dr. Moore stresses the importance of postgraduate training of the physician to keep him up to date. My own observations have convinced me that we need less of the display of modernity than we do of stressing such elementals as the anatomy and physiology of pregnancy and labor, as well as the necessity for aseptic technique, adequate diagnosis of the normal, and proper appreciation of the abnormal.

The postgraduate lecture seminars of many of our State Medical Societies feature too largely, in many instances, the academic, the laboratory, the exceptional, the abstractly scientific phases of obstetrics. The practicing physician may believe that he needs "brushing up," but it is doubtful, to me at least, whether an abstruse evening lecture by a visiting specialist will afford him much satisfaction or actual benefit. I rather lean to and have advocated in my own state a visit of from a few days to perhaps a week to a teaching center with attendance at clinics, in wards, in the delivery room, places where he comes into contact with the actual patients. For the younger men, the brief residencies, to which Dr. Moore refers, are also most desirable, provided they are not affected too much by the "fancy" obstetrics witnessed and attempt them when they return. In my belief, it is the obstetric elementals which should be impressed.

I therefore agree with much of what Dr. Moore presents in his paper, and his suggestions might well be applied elsewhere. The maternal death rate in this country has declined in an extraordinary manner, and this is due, in my belief, to the analysis of its own work by the profession in the various study committees which have been developed over

TABLE I. THE USE OF PLASMA IN OBSTETRIC PATIENTS FROM AUGUST 27, 1944, TO AUGUST 27, 1945

	PATIENTS	UNITS
Ectopic pregnancy with severe hemorrhage	9	16
Placenta previa	16	27
Postpartum hemorrhage	64	92
Abruptio placentae	2	2
Cesarean section	3	8
Abortion	18	22
Vaginal bleeding	2	4
Total	114	171

TABLE II. THE EXTENT TO WHICH PLASMA HAS BEEN USED THROUGHOUT NORTH DAKOTA DURING THE FIRST YEAR OF OPERATION OF THE PLASMA BANK

Total communities in which one or more units of plasma has been used	38
Total number of counties in which plasma has been used	32
Total reports received on units of plasma to date	1,250
Total number of patients receiving plasma	663

TABLE III. DISTRIBUTION OF PLASMA

Hospitals	44	
Physicians	31	
Drugstores	3	
Total depots	78	
Total number of counties in North Dakota*		53
Total number of counties having plasma		49
Counties with no hospital or physician		3

\*One total county is Indian Reservation.

TABLE IV. TOTAL COST OF PROGRAM

Total cost of program to date	\$26,572.14
Cost per unit of plasma since the beginning of the program	12.56
Estimated cost per unit for the coming year	
Minimum	2.75
Maximum	3.00

The distribution of the plasma throughout the state is of interest because it again calls attention to the factor of environment. Table III gives that distribution.

The total cost of the program during its first year of operation and the anticipated cost of plasma in the future are of interest and appear in Table IV.

I have used the plasma bank as another illustration of how environment can be changed with resultant good, not only to the practice of obstetrics, but to the general practice of medicine and surgery.

Our next and, I believe, our most far-reaching and important step in changing the environment will be the establishment of a four-year medical school at the University of North Dakota. We were successful in getting the last session of the North Dakota Legislature to pass an enabling act, authorizing the establishment of a Medical Center at the University of North Dakota. I visualize the integration of a number of the established hospitals throughout the State into a teaching program with the University and giving the medical students in the University firsthand insight into the problems of medical prac-

## ENDOLYMPHATIC STROMAL MYOSIS\*

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*(From the Departments of Obstetrics and Gynecology and Pathology of the University of Toronto)*

THIS paper is a report of a clinical and pathologic study of seven unusual uterine tumors arising from the endometrial stroma. Five of these tumors were received from the gynecological service of the Toronto General Hospital, one from the Wellesley Hospital, Toronto, and one from the St. Catharines General Hospital, St. Catharines, Ontario. The tumors are identical in most of their histologic and pathologic characteristics. They are composed of cells which closely resemble the cells of the endometrial stroma. They spread by direct extension between bundles of uterine muscle, along perivascular and perilymphatic tissue spaces, and within the lumen of both vascular and lymphatic channels. These histologic characteristics identify them as similar to neoplasms that have been described by Casler,<sup>1</sup> Frank,<sup>2</sup> Goodall,<sup>3</sup> Miller and Tennant,<sup>4</sup> and Robertson and his co-workers.<sup>5</sup>

In 1919 Casler, the first to report this type of neoplasm, described it as "a unique diffuse uterine tumor, really an adenomyoma with stroma but no glands." In his case the tumor obviously arose from the endometrial stroma and had diffusely invaded the uterine wall in a manner similar to adenomyoma. In 1932, Frank reported three cases similar in histologic appearance to the one of Casler, but exhibiting a spread almost completely confined to peri- and intralymphatic channels. Frank described the close resemblance between the tumor cell and the endometrial stroma cell, but could not demonstrate a direct continuity between the endometrium and the tumor. In 1937, Goodall reported fourteen cases presenting gross and microscopic features, which closely allied them to the cases previously reported by Frank and Casler. He suggested the name "stromal endometriosis" for these tumors. Since 1937, nine more cases have been reported, three by Miller and six by Robertson.

These authors have all described their cases in detail. Nevertheless, the rarity of the lesion, its uncertain malignancy, and unusual pathologic characteristics would seem to warrant this present report. The first of our seven cases was encountered in 1933, the last in 1942. The original pathologic diagnosis in all cases was endometrial sarcoma.

### Pathology

In all cases, the uterus contained one or more tumor masses, which, depending on their size, situation, and number, caused regular or irregular enlargement of the uterus. The largest uterus contained multiple tumors and measured 24 cm. in its widest diameter (Fig. 1). The smallest contained a single tumor

\*Read (by invitation) at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

the country. But we must not stop with achieving a lower mortality rate; the avoidable complications and accidents, and morbidity likewise must be reduced.

Dr. Moore stresses environment as a factor in the successful conduct of obstetric procedures. In large measure this is true, but no matter what the material environment may be, the actual criterion of success is the knowledge and ability which reside in the doctor who has assumed the responsibility of bringing the woman successfully through her pregnancy and labor. He in a sense is the one who creates the environment. I feel that Dr. Moore and his group should be highly commended for their efforts to inculcate in their region an appreciation of good obstetric care.

DR. RUDOLPH A. BARTHOLOMEW Atlanta, Ga.—Poor environment in obstetrics, as so well pointed out by Dr. Moore, is not so much a matter of geography as it is a matter of lack of physical equipment and obstetric skill and judgment. It is not enough to supply modern physical facilities, for these, in the absence of obstetric conscience, skill, and judgment actually tend to worsen obstetric morbidity and mortality through temptation to use unwarranted operative procedures.

Step by step, in logical sequence, the essayist has traced the essentials of good obstetrics, from thorough basic undergraduate training to continued postgraduate instructions through the years of practice, to sustain interest and help the practitioner reach greater obstetric proficiency.

In lieu of compulsory periodic renewal of licensure, which some have advocated to insure that practitioners keep abreast of progress in medicine, it would seem far better to provide facilities for compulsory refresher postgraduate instruction to accomplish the same end.

The success attending the writer's efforts to integrate all agencies, State Health Department, lay and professional, having as their objective improved obstetric care, is reflected in the lowered infant and maternal mortality rate.

It occurs to me that the State Boards of Health could furnish a much needed service by appropriating funds to subsidize free consultation by long distance telephone, for practitioners confronted with obstetric problems of emergencies. Well-qualified obstetricians, preferably members of the American Board of Obstetrics, could be appointed to serve as consultants. The state could be divided into districts, each of which could be served by a consultant and his alternate for a certain period of time.

It is my belief that practitioners would welcome such a service, and that much good could be accomplished in directing the proper management of the case and benefit both the patient and the practitioner.

Dr. Moore's paper brings home to us the fact that whatever is of practical value in original research, or papers presented before our special societies, must depend for its dissemination and ultimate benefit on facilities such as he has pioneered in North Dakota.

DR. MOORE (Closing).—As to the question of the nurse-midwife, in 1940 our physicians delivered 94 per cent of the obstetric patients in North Dakota, and in 1945 they delivered 99 per cent of them. Thus far we have not had to resort to nurse-midwife deliveries in very many cases. If our decline in the number of physicians continues, we might have to use more midwives than we have in the past.



with clear fluid were present in the larger tumor masses in three separate specimens. In one specimen extensive interstitial hemorrhage had occurred into the largest tumor which filled the endometrial cavity. Radiating out from these large tumors were cords and islands of tumor tissue infiltrating the myometrium. For the most part, they appeared to lie in vascular and lymphatic channels (Fig. 3). They stood out prominently above the cut myometrial surface of the fresh specimen, and could be squeezed out or pulled free as slender worm-like strands of rubbery tissue. Extension beyond the boundaries of the uterus into the broad ligaments was grossly evident in five cases. This was particularly noted in the areas about the uterine vessels where fingerlike strands of tumor protruded from the cut vessels.



Fig. 3.—Case 7. Sagittal section of uterus in Fig. 2 showing infiltration of the posterior wall of the uterus by cords of tumor, the majority of which are in lymphatic channels.

Microscopically, these tumors were composed of cells which for the most part closely resemble the endometrial stromal cell of the late proliferative phase. The cells were remarkably uniform in size, shape, and staining qualities. In some areas, a fibrouslike appearance of the tumor cell was noted, a change similar to that which is frequently observed in the stroma of the endometrium in endometrial polypi. In one specimen, that portion of the tumor which partially filled the endometrial cavity showed a moderate degree of anaplasia hyperchromatosis and an occasional mitotic figure. Areas of edema, myxomatous-like degeneration, and the formation of varying sized cystic spaces were also observed. A most characteristic microscopic feature of the tumor is the presence of numerous thick-walled blood vessels resembling the spiral arteries of the endometrium. The vessels varied from small capillaries to thick-walled muscular arteries, and were strikingly evident in all sections (Figs. 4 and 5). The large tumor masses were not encapsulated and were in direct contact with the uterine wall, forming a slightly irregular tumor myometrial junction similar to that of the normal endometrium. A varying degree of myometrial hypertrophy was evident in only three specimens, and in none was it present to a marked degree.

The myometrium was invaded by broad and slender cords of tumor extending between muscle bundles and along perivascular and perilymphatic tis-

measuring 6 cm. in diameter. These tumors were subserous and interstitial in situation, and in all but two cases formed, as well, varying sized sessile and polypoid tumors, which partially filled the endometrial cavity (Fig. 2). They were nonencapsulated, of soft brainlike consistency, and on section were faintly yellow in color and of homogeneous, velvety texture. Small cystic spaces filled

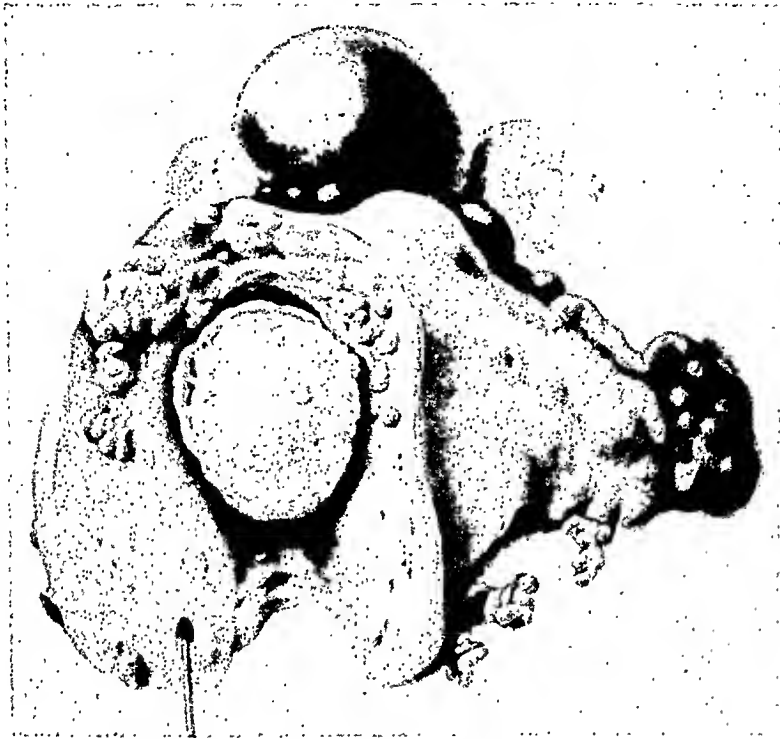


Fig. 1.—Case 1. Uterus enlarged by multiple tumor masses. The broad ligament lymphatics are nodular and distended with fingerlike processes of tumor which are protruding from the cut vessels. The probe indicates a distended lymphatic in the uterine wall out of which tumor has been pulled.



Fig. 2.—Case 7. Uterine cavity filled with a polypoid tumor mass.

sue spaces (Fig. 6). These strands of tumor were frequently seen pushing their way into lymphatic channels while still covered by intact endothelium (Figs. 7 and 8). In most areas, however, they appeared as masses of tumor tissue lying free in lymphatic spaces (Fig. 9). Invasion of blood channels



Fig. 6.—Case 3. This section shows tumor growing between muscle bundles and within the lumen of a lymphatic channel ( $\times 46$ .)



Fig. 7.

Fig. 8.

Fig. 7.—Case 3. Tumor growing between muscle bundles and into a lymphatic vessel. ( $\times 120$ .)

Fig. 8.—Case 6. Tumor bulging into a lymphatic vessel but still covered by intact endothelium. ( $\times 320$ .)

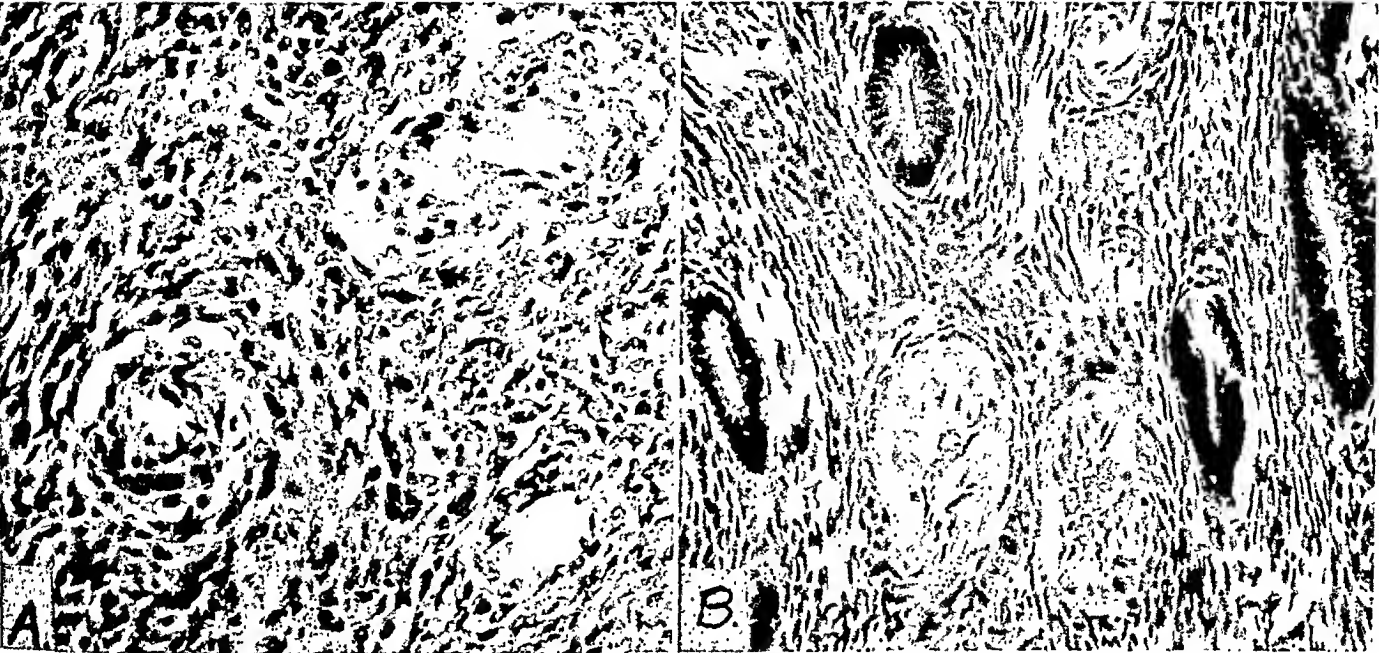


Fig. 4.—Case 6. A.—Section showing the thick-walled blood vessels which are a strikingly constant feature of the tumor. Comparison with the normal endometrium, section B, reveals the close resemblance between the cells and blood vessels of the tumor with the stromal cells and blood vessels of the normal endometrium. ( $\times 230$ .)

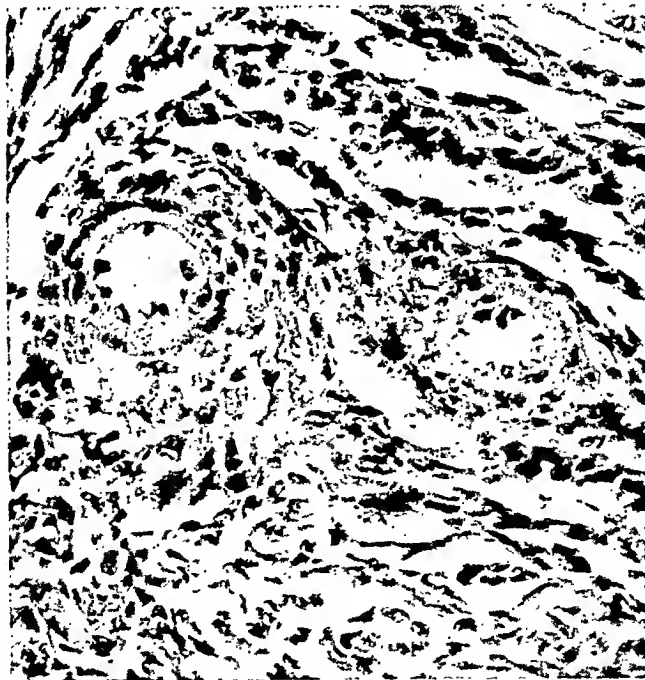


Fig. 5.—Case 6. Section of tumor removed from a lymphatic channel. ( $\times 320$ .)

pleted. Maternal indications for operative delivery (eclampsia, cardiac disease, and uterine inertia) may be approached conservatively. When operative delivery becomes necessary it should be performed with as little trauma to maternal and fetal tissues as possible. Extraperitoneal cesarean section may offer a better solution for some prolonged, infected labors than Dührssen's incisions followed by difficult forceps extractions. This is particularly true of those patients with "dystocia dystrophy syndrome," emphasized by DeLee. Women with intrapartum fever are apparently particularly predisposed to certain complications of labor. In this series, postpartum hemorrhage (over 600 c.c.) occurred in 21 patients; manual removal of the placenta was necessary on three occasions. The presence of these complications in febrile labors amplifies the dangers already present inasmuch as invasion of the birth canal may become necessary. Prior to the introduction of penicillin and the sulfonamides, manual removal of the placenta<sup>1</sup> after a febrile labor of genital origin often resulted in maternal death from sepsis. Probably the vigorous use of the newer antibiotics significantly reduces this risk. In febrile labors with genital infections, episiotomy wounds and perineal lacerations sutured with catgut are apt to disrupt; silkworm gut<sup>25</sup> has been recommended, since drainage is simplified after such repairs.

Grave significance has been attached to continued fever in the early puerperium<sup>1, 19</sup> since it may indicate a fulminating puerperal infection. Penicillin, sulfonamides, transfusions, and efficient nursing care constitute the basis for intelligent therapy. Attention should obviously be directed to the possibility of an extragenital cause of fever, and proper diagnostic procedures should be employed to clarify the clinical picture.

Infant pneumonia and bacteremia in the neonatal period are common, particularly in the presence of maternal genital infection with amnionitis. Penicillin or sulfonamide therapy commenced immediately after birth will save some infants. Recently, sulfathiazole (1½ grains per pound weight per twenty-four hours) was successfully employed in an infant with staphylococcus bacteremia. Penicillin should prove even more effective. Other neonatal infections (conjunctivitis, impetigo, and subcutaneous abscesses) occur and early adequate treatment must be instituted.

### Case Reports

CASE 1.—(E-9990.) M. G., aged 39 years, para v, gravida ix, was admitted Feb. 6, 1931, approximately eight months pregnant, in labor with an upper respiratory infection and a temperature of 103.6° F. After a short labor a 2,200-gram stillborn infant was delivered spontaneously. Immediately, postpartum signs of pneumonia appeared and death occurred twenty-eight hours after delivery. Hemolytic streptococci were recovered from blood taken just before and after delivery. Autopsy was refused; streptococcal septicemia was the probable cause of death.

CASE 2.—(F-3815.) M. K., aged 31 years, para 0, gravida i, was admitted May 17, 1931, at term. She was irrational, with a pulse rate of 150 beats per minute, temperature 102° F., absence of fetal heart sounds, three plus albuminuria, edema of fundi, and fully dilated cervix. A 4,225-gram stillborn infant was extracted with forceps. The amniotic fluid was infected and foul. Shock,

could be demonstrated with less frequency than invasion of lymphatics, due in part to the difficulty of differentiating between capillaries and lymphatics. Vascular invasion, however, could be established readily when the invaded vessel was thick-walled or contained a sufficient number of red blood cells to identify it as a blood vessel (Fig. 10). The lymphatics and wall of the Fallopian tube were infiltrated in two cases, and in one of these the subserous venous channels also were distended with tumor (Figs. 11, 12, and 13).

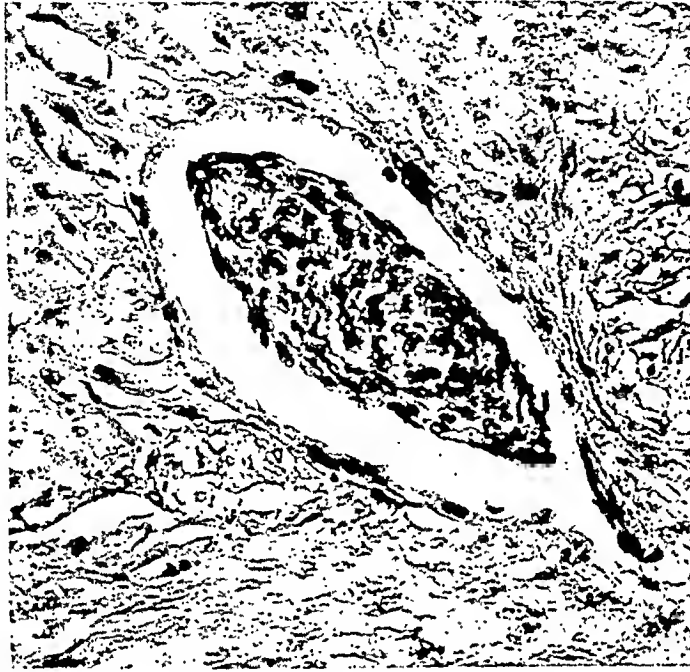


Fig. 9.—Case 6. Tumor within the lumen of a lymphatic channel. ( $\times 480$ .)

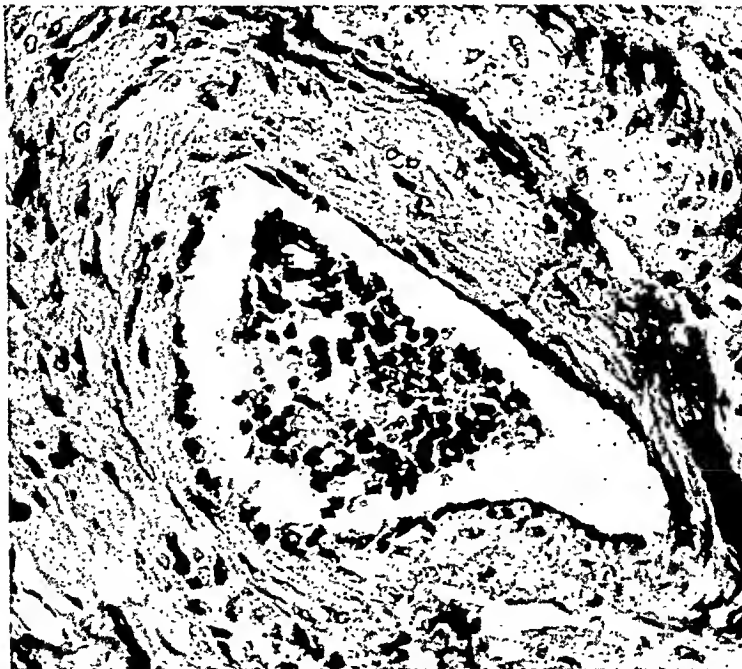


Fig. 10.—Case 3. Tumor within the lumen of a blood vessel. ( $\times 300$ .)



Direct continuity between the endometrium and the intramural tumor was evident in five cases. In two cases, despite a diffuse involvement of the posterior wall of the uterus, no such continuity could be shown. In both of these cases the tumor could be traced within a few millimeters of the basal layer of the endometrium, yet, despite multiple sections, direct continuity could not be established.

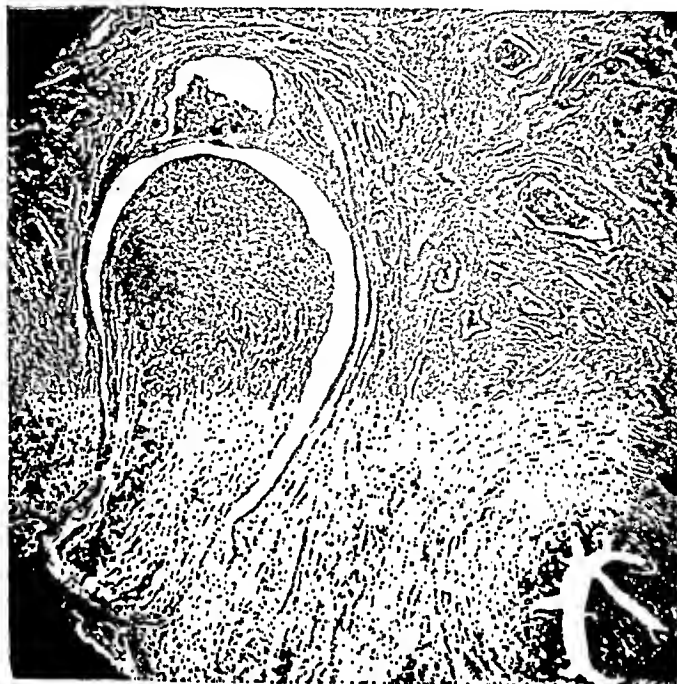


Fig. 11.—Case 3. Section of Fallopian tube showing infiltration of its wall by tumor. The lumen of the tube is at the lower right of the photomicrograph. Small capillaries above the tubal lumen are filled with tumor, and to the left a large mass of tumor pushing into and dilating a lymphatic channel is evident. (X20.)



Fig. 12.—Case 1. Lymphatic vessels of the broad ligament filled with cords of tumor. (X20.)

A great number of sections from all seven cases were examined, and in only one instance were endometrial-like glands encountered in the intramural or subserous portions of the tumor. These were found in a block cut from a large subserous tumor in Case 6. They comprised a clump of three typical endometrial glands of the proliferative phase. It is possible that they arose from invaginations of the serosal covering in the subserous tumor by a process of metaplasia of the serosal cells. Glands were occasionally encountered near the surface of the sessile and polypoid tumors in the endometrial cavity. These probably represented remnants of the endometrium, which originally had covered the surface of the polypus.



Fig. 13.—Case 2. Tumor within the lumen of two subserous veins. ( $\times 20$ .)

Sections were stained to demonstrate reticulum using Laidlaw's silver stain. They showed a basket-weave network of the reticulum surrounding the individual tumor cell similar to the reticular pattern of the endometrial stroma.

### Clinical Features

An analysis of the clinical histories of these cases failed to reveal symptoms or signs that could be considered distinctive for this type of tumor.\* In one case, menstruation was undisturbed. In the remainder, bleeding was irregular and profuse. The blood loss was quite severe, as in five of these the hemoglobin estimation was less than 50 per cent. In one case, the symptoms due to the presence of the tumor were masked by a tuberculous salpingo-oophoritis and pelvic peritonitis. The age of the patients varied from 28 to 45 years. Parity was widely varied, from para 0 to para vii.

\*The clinical features of the cases are summarized in Table III.



TABLE I. AGE AND PARITY

CASE NO.	AGE (YEARS)	PARITY
1	32	3
2	37	2
3	44	7
		(13 abortions)
4	47	2
5	28	0
6	45	4
7	45	0

The essential finding on examination was enlargement of the uterus. This enlargement was irregular in six of the seven cases, and led to a diagnosis of fibromyomas. In two instances it was recognized that the uterine tumors were of softer consistency than the usual myoma, and a diagnosis of degenerating fibroid was made.

All seven cases were subjected to bilateral salpingo-oophorectomy and hysterectomy. The findings at the original laparotomy in three cases did not excite the suspicion of the surgeon that he was dealing with an unusual type of uterine tumor. In the remaining four cases it was immediately evident that a most unusual lesion was present. The broad ligament lymphatics were enlarged, ropey, and hard. In one case extension could be palpated in the perivascular lymphatics of the left ovarian artery up to the renal vessels. The infundibulopelvic ligaments were thickened, and when clamped and cut, wormlike masses of tumor squeezed out between the clamps. The same thing again occurred when the uterine vessels were severed and the uterus amputated. In these four cases the condition appeared to be beyond the hope of surgical cure and the operation was completed as a palliative measure. The uterine tumor masses were covered by smooth glistening peritoneum, and there was no evidence of secondary peritoneal implantation of tumor cells. Peritoneal adhesions were absent in five cases. In two cases adhesions were numerous, but in one were due to previous laparotomy for ruptured appendix, and in the other to tuberculous salpingitis. There were no findings suggestive of endometriosis.

One patient originally had a supravaginal hysterectomy and left salpingo-oophorectomy. Following the pathologic diagnosis of sarcoma of the uterus, a second laparotomy was performed, and the remaining tube and ovary and cervix were removed. The patient with tuberculous salpingitis had, in all, four laparotomies. At the first, the tuberculous adnexa only were removed, due to the poor general condition of the patient and operative difficulties. The uterus, at this time, was thought to contain ordinary fibroids. One year later, due to uterine bleeding, a second operation was performed and the uterus was removed. Two and a half years later a recurrent tumor was removed from the retroperitoneal cellular tissue. Eight months later, and four and a half years after the original operation, a fourth laparotomy was performed for large bowel obstruction due to another local recurrence. A colostomy was done. The patient died five months later. Unfortunately, a postmortem examination was not permitted.

Five of the seven patients received postoperative high voltage x-ray therapy. Three of these received high voltage at 400 kilovolts; 100 cm. distance; 30 treatments through five pelvic ports, two anterior and three posterior, to 1,800 R per port. In addition, one of these five patients received 15 treatments through the vaginal cone to 3,000 R. In the remaining two cases, high voltage at 200

kilovolts, 50 cm. distance, was employed. One received 1,200 R per port, the other 1,600 R and, in addition, 1,100 R through four abdominal ports to cover the whole abdomen.

The follow-up record for all cases is shown in Table II, and reveals that six patients are alive and well, and one has died from recurrent disease.

TABLE II. FOLLOW-UP RECORD

CASE NO.	DURATION OF FOLLOW-UP (YEARS)	STATUS
1	9	Alive and well
2	9	Alive and well
3	7	Alive and well
4	7	Alive and well
5	3	Alive and well
6	6	Alive and well
7	5	Dead

### Discussion

These tumors possess characteristics which make them difficult to classify as either benign or malignant. The tumor cell is a well-differentiated mature type of cell, showing an absence of anaplasia hyperchromatosis and mitotic figures, all of which denote benignancy. The presence of thick-walled blood vessels, a strikingly constant feature of the neoplasm, suggests slow growth, a characteristic usually associated with benign tumors. The manner of invasion of the uterine wall by pushing between muscle bundles and along perivascular tissue spaces without actual destruction of muscle resembles the myometrial invasion of adenomyosis rather than sarcoma. The widespread invasion of lymphatic channels and, to a lesser extent, of blood vessels, however, is an attribute of sarcoma, and sets the stage for the occurrence of distant metastatic growths that are characteristic of malignant neoplasms. That distant metastases have not been an accompaniment of these tumors is surprising. The tumor, when pulled from lymphatic channels, is not in the least friable, but of rather rubbery consistency, a characteristic that may explain the absence of embolic metastases.

It was grossly evident in six cases that surgical removal of the tumor had been incomplete, yet five of these patients are alive and well after six to nine years. This failure of the tumor left in situ to continue its growth is difficult to explain. Four of the five patients received high voltage x-ray and one did not, yet all have survived to the present. The mature, well-differentiated tumor cell would not ordinarily be considered as particularly radiosensitive. Goodall, who considers the lesion a type of endometriosis, believes that its growth is dependent upon estrogen stimulation from the ovary. All of our cases had bilateral oophorectomy. Yet, in one the tumor continued to grow, and the patient eventually died from massive local recurrence. Of Goodall's two fatal cases, one had bilateral oophorectomy, and the other received radium and high voltage x-ray therapy that ordinarily would destroy the secretory function of the ovaries. The abundance with which the tumor is supplied with capillary and larger blood vessels suggests that it may be dependent on its own vascular system for nourishment and growth, and that extensions beyond the uterus into the broad ligament lymphatics are like the branches of a tree rather than its

TABLE III. CLINICAL SUMMARY

CASE NO.	AGE (YEARS)	PARITY	SYMPTOMS	OPERATIVE TREATMENT	EXTENSION OF TUMOR BEYOND UTERUS	X-RAY THERAPY	FOLLOW-UP
1	32	III	Abdominal tumor for 6 months	Bilateral salpingo-oophorectomy; supravaginal hysterectomy	Yes	200 K.V.	Alive and well, 9 years
2	37	II	Vaginal bleeding for 4 years; hemoglobin 40%	Bilateral salpingo-oophorectomy; supravaginal hysterectomy	Yes	200 K.V.	Alive and well, 9 years
3	44	VII 13 abortions	Irregular vaginal bleeding. Abdominal tumor for 6 months. Hemoglobin 80%	Bilateral salpingo-oophorectomy; supravaginal hysterectomy	Yes	400 K.V.	Alive and well, 7 years
4	47	II	Profuse and irregular vaginal bleeding for 3 months. Hemoglobin 45%	Bilateral salpingo-oophorectomy; total hysterectomy	No	400 K.V.	Alive and well, 7 years
5	28	0	Vaginal bleeding for 2 months	1. Supravaginal hysterectomy; left salpingo-oophorectomy 2. One month later, rt. salpingo-oophorectomy and removal of cervix	Yes	400 K.V.	Alive and well, 3 years
6	45	IV	Vaginal bleeding for 4 months; hemoglobin 40%	1. Diagnostic curettage 2. Bilateral salpingo-oophorectomy; supravaginal hysterectomy	Yes	No	Alive and well, 6 years
7	45	0	Vaginal bleeding: I. Pelvic pain: Chills and fever. (Tuberculous salpingitis) II. Vaginal bleeding III. Recurrent tumor IV. Intestinal obstruction	1. Bilateral salpingo-oophorectomy 2. Total hysterectomy, 1 year later 3. Removal of recurrence 2½ years later 4. Colostomy, 8 months later	Yes	No	Died, 5 years

roots. Thus, unless the extensions develop secondary vascular attachments, hysterectomy would result in a severance of their blood supply, ischemia, and death.

All of our cases and most of those in the literature were originally diagnosed as sarcoma. This diagnosis was probably made on the widespread invasion of lymphatics rather than on cytology. Goodall describes a benign and malignant type of stromal endometriosis, but this differentiation appears to rest on

the clinical course of the disease rather than on histologic criteria. Robertson included a case in his series which exhibited many characteristics of stromal myosis, but showed also cellular pleomorphism and necrosis. He designated the tumor as a malignant stromal endometriosis, but unfortunately, the case was too recent for a follow-up to have been made. Goodall's fatal cases died ten and eleven years after initial operation, while in Frank's case recurrence took place seventeen years after the removal of the primary tumor. It would appear that the lesion should be considered of low-grade malignancy with a tendency to late local recurrence.

The relationship of this tumor to endometriosis is uncertain. Goodall believes that the relationship is a close one, and considers the lesion as one type of endometriosis. Casler's case eventually developed an endometrial cyst of the ovary, and five of Goodall's cases were associated with ovarian endometriosis. These, however, were not all substantiated histologically. In our cases there were no clinical or pathologic findings suggestive of ordinary endometriosis, except in the one case which showed a small clump of three endometrial-like glands in a large subserous tumor. The growth differs from endometriosis rather markedly, however, in at least four major respects: it does not menstruate; it forms large, solid tumor masses; it extends along lymphatic and vascular channels by direct continuity of growth; it tends to recur many years after initial removal. These differences would appear to be of sufficient magnitude to warrant the recognition of the lesion as an entity distinct from endometriosis.

It is difficult to find a short descriptive name for the lesion. Frank, in 1932, suggested "endolymphatic fibromyosis," which has the disadvantage of not denoting the stromal origin of the tumor. A simple change of his descriptive name to "endolymphatic stromal myosis" retains the advantage of Frank's nomenclature, and has the added value of denoting the origin of this unusual tumor.

### Summary

The clinical histories, follow-up records, and pathologic characteristics of seven cases of rare uterine tumors arising from the endometrial stroma are presented. They are similar to cases that previously have been described as adenomyoma without glands, endolymphatic fibromyosis, and stromal endometriosis. They exhibit pathologic characteristics, which in the past frequently have led to a diagnosis of endometrial sarcoma. They seem to be of low-grade clinical malignancy. Due, however, to the late recurrences which have been reported, long follow-up records are necessary before the degree of clinical malignancy of these tumors can be assessed. They occur during the years of sexual maturity and present signs and symptoms similar to those of uterine fibromyomas. Their relationship to endometriosis and adenomyosis is uncertain. Their pathologic and clinical characteristics are sufficiently distinctive, however, to warrant their separate classification. "Endolymphatic stromal myosis" is suggested as a name for these neoplasms.

I am indebted to Drs. W. G. Cosbie, C. O. White, and Roscoe R. Graham for the clinical histories and follow-up records of their private cases. I am also indebted to Dr. G. W. Lougheed, pathologist, Wellesley Hospital, Toronto, and to Dr. Lorne Whitaker, pathologist, St. Catharines General Hospital, St. Catharines, for the opportunity of studying their surgical

specimens. The high voltage x-ray treatments were given under the direction of Dr. Gordon Richards, radiologist, Toronto General Hospital, and Director of the Ontario Institute of Radiotherapy, Toronto.

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### Discussion

DR. RICHARD W. TELINDE, Baltimore, Md.—Dr. Henderson has described, and again called our attention to an uncommon uterine disease, but it is a disease of which the recognition and proper handling become of the greatest importance to the individual who suffers from it. In our experience it is very rare, despite Dr. Goodall's published statement to the contrary. In our laboratory, where 65,000 specimens have been examined, we have encountered only four cases, including the first one published by Casler. Two of these were our own and two were sent in from other clinics. As further proof of the rarity of the disease, it should be noted that in most of the small series reported, including that of Dr. Henderson, the cases have been collected from more than one clinic. During these years while we have encountered these four cases, we have seen 128 cases of sarcoma of the uterus in its various forms. Of these, 79 occurred in myomas, 11 in the myometrium, 11 in the cervix, and 27 in the endometrium. So, again I cannot agree with Dr. Goodall when he states that in contrast to his views on "endometrioma interstitiale," "sarcoma of the uterus is a very rare disease." Of course, one might argue that we are confusing the two conditions, but the differentiation is quite distinct.

There are two very important points relative to this disease. Dr. Henderson has mentioned both of them:

1. Its degree of malignancy.
2. Its relation to endometriosis.

In relation to malignancy, there are two things which are quite evident.

1. Many women do not die, in spite of incomplete removal. The analogy mentioned by Dr. Henderson to the withering of the branches of a tree after cutting the trunk is quite appropriate.

2. On the other hand, some cases do recur with metastases, some of which are controlled by irradiation, and others are not. Recurrences may be very late, as in Frank's case which recurred after seventeen years. A comparable degree of malignancy is found in granulosa tumors of the ovary. Recently, we have reported three cases with recurrence and death eighteen, twenty, and twenty-one years following the removal of the primary ovarian tumor.

Most writers have assumed this disease to be a special form of endometriosis. I am pleased that Dr. Henderson has taken a guarded view of this when he states, "The relation of this tumor to endometriosis is uncertain. On histologic examination of these tumors, one is struck with the similarity of them to adenomyosis of the uterus, but to my mind there are a few important differences which should put them into a different category:

1. Cases have been reported that have recurred and progressed following complete removal of ovarian tissue.

2. More important still is the fact that some of these tumors have made their clinical appearance years after the menopause. For example, Robertson reported one in a 55-year-old woman who began to bleed three years postmenopausally Miller reported one appearing with rapid growth seven years after her last period. Our recent case caused postmenopausal bleeding at the age of 61 years, more than ten years after her menopause. I appreciate the possibility of an extraovarian source of estrogen, but the fact remains that true endometriosis does not act in a similar way after the menopause.

3. Furthermore, the percentage of malignancy is much higher in these tumors than in true endometriosis.

4. Finally, the extension of these tumors by the lymphatics is different from the mode of extension of endometriosis.

There is one point in the diagnosis of this disease which is of some practical importance. Since many of the tumors grow into the uterine cavity as well as into the myometrium, tissue may be obtained by curettage which will establish the diagnosis.

Finally, a word as to the proper terminology for this disease. As mentioned above, I believe one is not justified in assuming it to be a special form of endometriosis. I feel that the term "endolymphatic" should be omitted, because it also extends "perilymphatically" and through blood vessels. Therefore, I suggest that the disease be called "stromatosis." This term indicates that the condition arises in the endometrial stroma, the only proved etiologic fact that we have. In using this term, we must do so realizing that some forms are benign and others malignant, and that the histologic differentiation is difficult and, at this time, probably impossible.

DR. EMIL NOVAK, Baltimore, Md.—It is a well-known fact that certain types of sarcoma of the uterus, not necessarily endometrial, have a tendency to grow intravascularly and to penetrate the lymphatics. In extreme cases one can even pull out plugs of sarcoma tissue from the larger uterine vessels. I would be inclined to interpret Dr. Henderson's cases as representing low-grade sarcomas of endometrial origin. One or two of the gross pictures which he showed, especially Fig. 2, presented the massive polypoid intrauterine growth which so often characterizes endometrial sarcoma. His cases could scarcely be considered benign, since there was such extensive dissemination.

I would like to amend Dr. TeLinde's suggestion as to the terminology of these stromal growths. For the benign group, the designation of benign stromatosis has been suggested, but I believe that it is unwise to separate this type from what may be called the mother group of adenomyosis, of which they represent one variety, and a rare one at that. They are better spoken of as stromal adenomyosis. Incidentally, such a diagnosis should not be made unless numerous sections establish that the stromal tissue invading the uterine musculature is not accompanied by glands.

There is even more valid objection to the term "malignant stromatosis," also recently introduced into the literature. Stroma is a connective tissue, and the malignant connective tissue tumor is sarcoma. The malignant prototype of the so-called benign stromatosis is endometrial sarcoma, and this is what such tumors should be called. It is both unnecessary and confusing to introduce such terms as malignant stromatosis.

DR. JAMES R. MILLER, Hartford, Conn.—I recently saw a patient who presented a picture almost identical with that mentioned by Dr. Henderson. She was 38 years of age, had three children, and had lost a great deal of blood during the previous nine months, so that her hemoglobin had sunk to 40 per cent. Total excision of the uterus, tubes, and ovaries was done. Complete removal of all tumor tissue was impossible, as it extended high on each side, in fact, to the level of the kidney vessels.

One point I think is worthy of mention, and it may have some bearing on nomenclature. The silver differential stain for stroma in these tumors shows the typical basket-work pattern which is characteristic of endometrial stroma. The similarity is so striking that it leads me to believe that the derivation of these tumors from endometrial stroma should be considered when naming them.

DR. HENDERSON (closing).—Regarding the incidence of these tumors, we collected our cases over a period of nine years from three different hospitals. Four of the cases occurred at the Toronto General Hospital.

I think the discussion of Dr. TeLinde and Dr. Novak emphasized my opening remark when I said these tumors are difficult to classify as either benign or malignant. I think "stromal myosis" is preferable to the name suggested by Dr. Novak of "stromal adenomyosis," as this definitely implies the presence of glands in the tumor. Dr. TeLinde's suggested name is quite descriptive.

# THE VALUE OF PLASMA PITOCINASE DETERMINATIONS IN OBSTETRICS\*†

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IN THE blood of pregnant women there is an enzyme which destroys the oxytocic properties of pitocin. Until this protein is purified and characterized as to specificity and action we may refer to it simply as "pitocinase." In this study, it will be shown that the level of plasma pitocinase is a guide to both the existence and the duration of pregnancy, and that variations from the normal range point to a basic enzymatic disturbance associated with eclampsia.

## Literature

The observation that pregnancy serum inactivates the posterior pituitary hormone was made by von Fekete in 1930.<sup>1</sup> Two years later, he showed that the oxytocic effect was reduced when the incubated mixture was tested on pregnant women, as well as when it was assayed on the isolated uterus of a guinea pig.<sup>2</sup> In 1935, Schockaert and Lambillon<sup>3</sup> demonstrated that pregnancy serum was also "antagonistic" to the vasopressor activity of postpituitary extracts, and that normal pregnant women were relatively insensitive to the blood pressure raising properties of this hormone,<sup>4</sup> a fact independently confirmed by Dieckmann and Miehle.<sup>5</sup>

The enzymatic nature of this reaction was not elucidated until 1941, when Werle and his co-workers<sup>6-8</sup> studied the inactivating power of pregnancy blood upon both pitocin and pitressin. They demonstrated the enzyme "in the second month of pregnancy" and said that the amount "remains at a fairly constant level from the third to the eighth month, is highest at birth, and can no longer be demonstrated one month afterward." They could not detect any in the serum of nonpregnant women nor in fetal cord blood, but found traces of activity in all urine specimens and in colostrum. The optimum pH for activity was between 6.5 and 7.5. The enzyme was thermolabile and easily oxidized, but after oxidation it could be reactivated by cysteine or glutathione. No inhibiting substances could be found.

In order to understand the type of reaction with which we are dealing, we must consider our substrate. The chemistry and physiology of the posterior pituitary hormones has been reviewed recently by Irving.<sup>9</sup> Pitocin (oxytocin, alpha hypophamine) is a polypeptide containing at least five amino acids, has an active sulfhydryl group and a molecular weight somewhere between 600 and 2,000. It is either separated or split off by chemical treatment from a large "mother" protein molecule which contains oxytocic, pressor, and antidiuretic properties in a constant proportion. When one of the peptide linkages of pitocin is split by enzymatic action, the substance loses its pharmacologic properties. Whether the oxytocic hormone of the posterior pituitary gland plays any role in the normal physiology of human reproduction has never been elucidated.

The following enzymes will *not* destroy pitocin: Crystalline trypsin,<sup>10</sup> carboxypeptidase<sup>11</sup> and pepsin;<sup>12</sup> concentrated preparations of bone phos-

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†Supported by the John and Mary Markle Foundation and the James Foundation Grant.

fever, and pulmonary congestion developed in the immediate puerperium and death occurred on the ninth postpartum day. Blood cultures were negative. Autopsy was refused.

CASE 3.—(F-10567.) L. W., aged 30 years, para iii, gravida iii, was admitted Jan. 7, 1932, near term. Shortly afterward, sharp, continuous, lower abdominal pain and temperature of 101° F. developed. Rectal examination revealed a firm, orange-sized mass behind the cervix; a 2,750-gram living infant was delivered by cesarean section. Peritonitis was present at operation and subtotal hysterectomy was performed. The patient expired on the third post-operative day of peritonitis. At autopsy an adenocarcinoma of the sigmoid and generalized peritonitis were found.

CASE 4.—(H-19.) L. G., aged 40 years, para iv, gravida vi, was admitted Jan. 2, 1933, in labor with a respiratory infection, cough, hemoptysis, and fever of 102° F. A 2,958-gram living infant was delivered spontaneously after a short labor, but the patient expired eighteen hours post partum from pneumonia. Autopsy was refused.

CASE 5.—(M-5040.) H. C., aged 20 years, para 0, gravida i, was admitted in coma on Oct. 11, 1935, seven months pregnant. A convulsion had occurred five hours prior to admission. The temperature was 102° F., blood pressure 155/90, fetal heart sounds were absent. After artificial rupture of membranes (releasing 6,000 c.c. amniotic fluid), manual dilation of the cervix and internal podalic version, a 2,180-gram stillborn, anencephalic infant was extracted. Cyanosis and pulmonary consolidation developed immediately and death occurred forty-eight hours after delivery. Autopsy disclosed bilateral, confluent, lobar pneumonia and infarction of the anterior lobe of the pituitary.

CASE 6.—(M-426.) M. T., aged 31 years, para 0, gravida i, was admitted July 14, 1936, approximately eight and one-half months pregnant with pyelitis. After artificial rupture of the membranes, a 2,578-gram living infant was extracted with forceps. The temperature reached 102° F. during labor. Anemia, edema, cyanosis, dyspnea, and delirium complicated the puerperium, and the patient died on the twenty-fifth postpartum day. Autopsy disclosed pelvic thrombophlebitis and pulmonary infarction.

CASE 7.—(P-8969.) M. S., aged 39 years, para viii, gravida ix, was admitted Jan. 21, 1937, approximately eight and one-half months pregnant with an upper respiratory infection, anemia, and fever of 102.8° F. A 3,650-gram stillborn, macerated infant was extracted with forceps after a short labor. Cyanosis, pneumonic consolidation, high fever, and delirium followed delivery, and death occurred on the fourth postpartum day. No autopsy was granted.

CASE 8.—(E-3072.) E. M., aged 24 years, para ii, gravida iv, was admitted with latent syphilis Oct. 2, 1937, at term. After the fourth injection of neoarsphenamine, arsenical encephalitis developed. Labor commenced spontaneously the next day. A 2,588-gram living infant was extracted with forceps after maternal death. The temperature rose to 105.6° F. just before death. Autopsy disclosed edema of the brain, fatty metamorphosis of the liver, and pulmonary edema.

CASE 9.—(38-21502.) E. C., aged 43, para xii, gravida xiv, had elective premature artificial rupture of membranes at term. During a latent period of four days. Fever of 102.0° F. developed and the fetal heart sounds disappeared. After a short labor a 3,690-gram stillborn infant was delivered. There was a postpartum hemorrhage of 800 cubic centimeters. The ensuing febrile course



four hours after excision if kept in Tyrode's solution in the ice box. In matching responses, the mean rise rather than the peak of the elonic response is the more accurate reflection of the dose. Some typical responses obtained are illustrated in Fig. 1. The usual precautions of bubbling oxygen next to the strip, avoiding trauma to the uterus, neutralizing and warming all solutions to be tested, and counterbalancing the tension on the uterus carefully are all essential for performing the bioassay within an accuracy of plus or minus 25 per cent.

### Calculations

The destruction of pitoein by pregnancy plasma follows the kinetics of a first order reaction, and the log of the percentage remaining plotted against time gives a straight line. We have determined by repeated trials that the velocity of the reaction is independent of the amount of pitoein used and varies only with the concentration of the enzyme in the incubation mixture. Accordingly, if the time taken for half destruction is determined, the velocity can be calculated by applying the simple formula  $k = \frac{0.693}{\frac{1}{2} \text{ time (minutes)}}$ .<sup>14</sup> We have adopted

100 times  $k$  (the velocity constant) as the unit of pitoeinase activity, and when this is multiplied by the dilution of plasma utilized in the incubation, the result gives the units of pitoeinase per ml. of plasma. In order to estimate how much plasma to use and how long the incubation times should be, an approximate prediction of the activity must be made (from the curve of Fig. 2). The following derivation of the first formula is then useful:

$$\frac{\frac{1}{2} \text{ time (min.)}}{\text{plasma dilution}} = \frac{0.693 \times 100}{\text{estimated units/ml. plasma}}$$

A convenient incubation time is selected and the plasma diluted accordingly. Samples are removed at the estimated time for half destruction, about one-third less and one-third more than this time in order to obtain at least four points (the zero time sample being the first). Following the assay, the log of the percentage of pitoein remaining is plotted against time—most conveniently with semi-log paper—and by fitting a straight line through the four points, the time for half destruction may be easily read from the chart. Values of less than 0.1 units/ml. of plasma may be readily determined, but an activity corresponding to less than 0.05 units/ml. of plasma must be considered as doubtful.

### Results

*Nature and Stability of Plasma Pitocinase.*—The enzyme with which we are dealing is a large protein molecule, and most of the activity may be found in that fraction salted out at one-third saturation of ammonium sulfate. Attempts at purification are difficult because the activity is so easily destroyed by oxidation. A portion, but not all, of the lost activity may be restored by treatment with cysteine. Preliminary treatment of pregnancy plasma with 0.1 molar iodoacetate does not inhibit the activity. Prolonged incubations (over six hours) are best carried out in modified Thunberg tubes *in vacuo* with a heavy layer of toluene on the surface.

Pregnancy plasma may be stored at 6° C. overnight without appreciable loss of activity, but there is a loss of 60 per cent of the activity in four days at this temperature. If the plasma is frozen, or is kept at 6-8° C. *in vacuo* or

phatase,<sup>12</sup> amine oxidase, diamine oxidase (histaminase), and the fibrinolytic enzyme of activated human plasma (present study). Other enzymes, in variable concentrations, *will* destroy pitocin: Crystalline chymotrypsin and concentrates of yeast aminopolypeptidase, "angiotonase" (extracts of red blood cells or kidney),<sup>10</sup> tyrosinase,<sup>13</sup> papain, and the dipeptidases and aminopeptidases of intestine.<sup>12</sup> Gulland and Macrae<sup>12</sup> believe that the enzyme which actually destroys pitocin (i.e., "pitocinase") is not identical with any of these latter impure enzymes but is simply a contaminant.

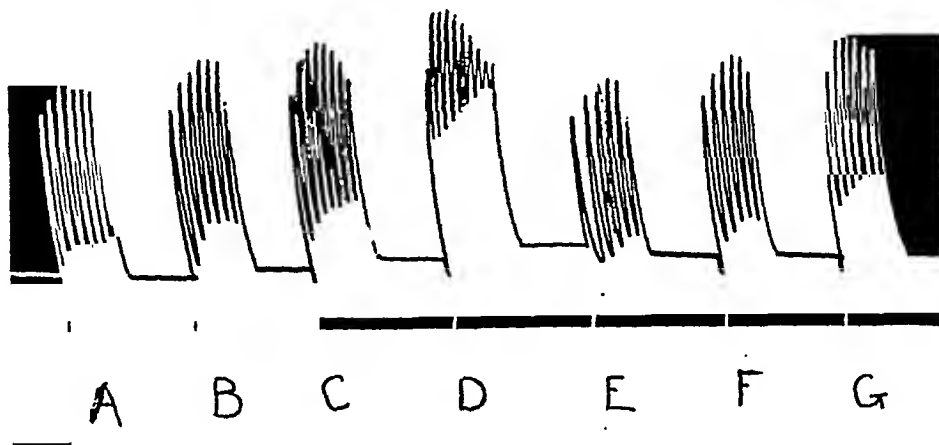


Fig. 1.—Response of isolated rat uterus to pitocin.

Tracing	Units added to 20 ml. bath	Mean rise (mm.)
E	0.01	17
A	0.025	20
B, F	0.05	22, 22
H	0.075	24
C, G	0.1	27, 28
D	0.2	37

### Methods

The technique of determining the plasma concentration of pitocinase is relatively simple. Five units (0.5 ml.) of commercial pitocin are added to a known amount of oxalated pregnancy plasma, the volume is made up to 50 ml., and a few drops of toluene are added as a preservative. An initial sample of 20 ml. is withdrawn and immediately inactivated by adding one drop of 10 per cent acetic acid and placing the tube in a boiling water bath for three minutes. The filtrate represents the "zero time" or "100 per cent substrate" standard with which subsequent samples are compared. The remainder of the mixture is incubated at 37° C., and 10 ml. samples are removed at predetermined intervals and inactivated in the same manner.

The percentage of pitocin remaining in each sample is estimated by a standard oxytocic assay on an isolated uterine strip suspended in Tyrode's solution in a constant temperature (37° C.) bath of 20 ml. capacity. For this purpose, we have used the uterine horns of rats too old to breed, or rats which have been castrated two to four weeks before use.\* The uteri are useful for twenty-

\*Castration or advanced age reduces the spontaneous motility of the isolated uterus without materially affecting its response to pitocin. In addition to its economy, the rat uterus has the advantage of being insensitive to histamine. As an interesting and puzzling side light, we have noticed that the uteri of castrated rats respond well to pitocin only if the animals are fed lettuce or vitamin A in addition to Purina Dog Chow, or are sensitized with estrogenic hormones. We have not as yet made a systematic study of this phenomenon, but the observation suggests that there is a relationship between vitamin A and the metabolism of the estrogens.

vary with the phases of the menstrual cycle, being high at the time of ovulation and very low during menstruation. The observed activity may be due to fluctuations of a nonspecific protease rather than to the more specific peptidase under consideration. Samples from 52 pregnant women, on the other hand, were positive in 51 instances and doubtful in one. The doubtful result (less than 0.05 unit/ml.) was obtained on a woman who was but sixteen days past the date of conception as judged from her basal body temperature curve.

The plasma of a rabbit, guinea pig, or rat did not show any activity during pregnancy. Five samples of fetal cord blood obtained at delivery showed no pitocinase activity.

Packed red blood corpuscles, after hemolysis, gave the same activity per gram as full-term pregnancy plasma, regardless of species or sex. The full-term human placenta, after brief extraction with saline in a Waring blender, exhibited from 30 to 50 units of pitocinase activity per gram of tissue. It is not known, however, whether pitocin may be destroyed by a variety of intracellular proteinases and peptidases, or whether the proteins extractable from tissues which destroy this substrate are identical with the plasma pitocinase of human pregnancy. The plasma enzymes which destroy angiotonin likewise increase in pregnancy, but to a much smaller extent, and there is no parallelism between "angiotonase" and "pitocinase" activity either in plasma or in tissue extracts.<sup>15</sup>

*Plasma Pitocinase in Normal Pregnancy.*—From the 4th to the 38th week after conception, there is a thousand fold increase in the plasma pitocinase concentration, and this high level is maintained during labor. Following delivery, the enzyme decreases logarithmically at the rate of about 25 per cent per day until it disappears in four weeks. Fig. 2 illustrates the rate of increase during normal pregnancy. (Four values of less than 0.1 unit/ml. do not show on this chart.) From the third to the sixteenth week after conception, there is a *100 per cent increase in plasma pitocinase concentration every twelve days*. Even though there were an error of 50 per cent in the bio-assay, one might therefore date the time of conception within plus or minus six days. The probable error of our bio-assay is within 25 per cent, and there does not appear to be much individual variation among women who are less than four months pregnant. During the last four months, the scatter is too great to make an accurate prediction of the date of confinement.

Following abortion, the same logarithmic decline of pitocinase concentration occurs that is noted after delivery; so that, if we know the date of abortion, we can calculate the approximate date of conception. Conversely, if we know how far advanced the pregnancy was, we can approximate the date on which the completed abortion occurred. Such information is limited in its usefulness, but might assume medicolegal importance. Of prognostic value, perhaps, would be the knowledge of whether the pitocinase level is increasing or decreasing after an episode of bleeding in the first trimester.

Twins (two cases), triplets (one case), and intrauterine death of the fetus (two cases) do not alter the values from the normal range.

*Plasma Pitocinase in Pre-eclampsia and Eclampsia.*—When true pre-eclampsia or eclampsia supervenes, an interesting phenomenon occurs (Fig. 3).

under a heavy layer of mineral oil, there is a loss of only 35 per cent in seven days. The results to be described below were all obtained with fresh blood samples.

*Distribution of Pitocinase.*—Plasma samples of 20 nonpregnant subjects, including amenorrheic and postmenopausal women, showed traces of pitocinase activity between the ranges of 0.01 and 0.06 unit/ml. of plasma. These values

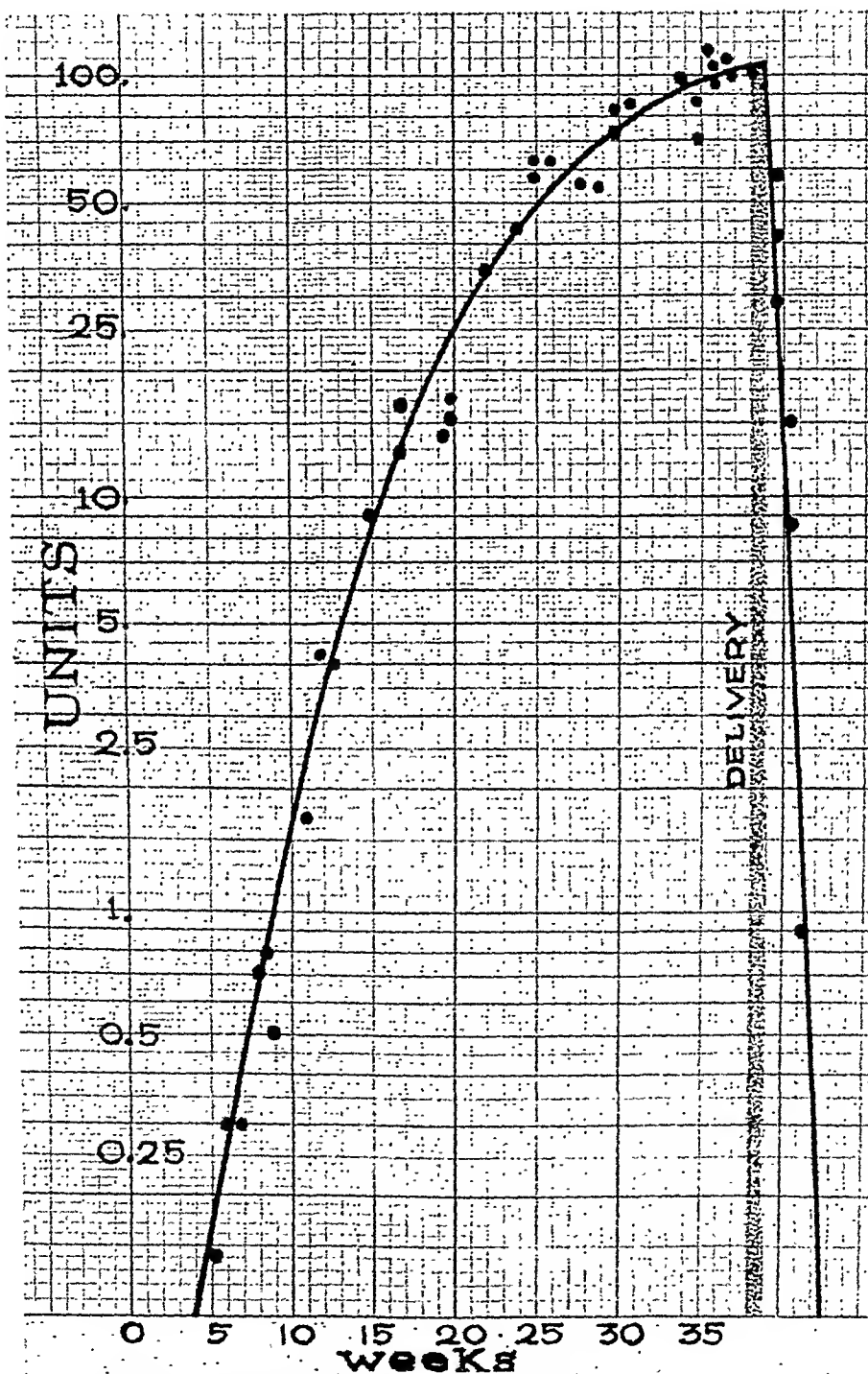


Fig. 2.—Plasma pitocinase levels in normal pregnancy.  
 Ordinate: Units/ml. plasma (values below 0.1 not illustrated).  
 Abscissa: Week of pregnancy, dating from conception.

taminase values are likewise scattered on both sides of the normal range, and again there is no apparent correlation between the value and the severity of the disease.\* The present observations, together with those of Ahlmark on histaminase<sup>16</sup> and Smith and Smith on serum fibrinolysin,<sup>18</sup> suggest that there is a basic enzymatic disturbance associated with eclampsia.

The source of plasma pitocinase in human pregnancy is not known, but the most reasonable hypothesis is that the trophoblastic syncytial cells contribute this protein to the maternal blood stream. The enzyme can be detected about three weeks after implantation of the fertilized ovum, and the rate of increase in the blood parallels the rate of growth of the placenta. The increase continues long after the histologic disappearance of the Langhans' cells. The protein is of sufficient size to prevent its passage into the fetal circulation. We have mixed the plasma samples from pregnant and nonpregnant women, and have found that the nonpregnant plasma acts as a diluent, in the same manner as saline solution. This would indicate that pitocinase does not exist normally as a zymogen which is simply activated by pregnancy blood. We know nothing about the physiologic significance of pitocinase, and it seems rather strange, speaking teleologically, that a woman is protected maximally against a natural oxytocic hormone at the onset of labor.

If both pitocin and pitressin are destroyed by the same enzyme, and even though all of the destruction were to occur in the plasma, as suggested for angiotonin,<sup>19</sup> it can be seen that a pitocinase concentration of 100 units/ml. in a normal pregnancy near term would permit the inactivation within forty-five seconds of half of any quantity of postpituitary hormone injected intravenously. This may account for the relative insensitivity of normal pregnant women to the blood pressure raising action of pitressin.<sup>4, 5</sup>

Since the uterine horns of an elderly female rat may be used for many tests at a negligible cost, the determination of plasma pitocinase may prove to be a rapid and economical test for pregnancy. Whether its accuracy approaches that of a urinary chorionic hormone determination remains for further study. With careful technique, the test has the additional advantage during the first four months of determining the week of pregnancy, and during the last four months it may be of value in the differential diagnosis of pre-eclampsia from other hypertensive disorders. At the present time, we are searching for some substrate other than pitocin, so that chemical or colorimetric titration may replace the more inaccurate and somewhat tedious bioassay.

### Summary

Very early in pregnancy, an enzyme capable of inactivating pitocin appears in the blood, and a method for its quantitative determination is described. The properties, kinetics, stability, and distribution of pitocinase are discussed.

During the first four months of human pregnancy, the plasma concentration of this protein increases logarithmically in such a fashion that not only the

\*As a tentative explanation, the essential change in pre-eclampsia may be an elevated level of both pitocinase and histaminase. In half or more of the cases, large protein molecules may be lost through the glomeruli, thus clearing the plasma of the enzymes at a rate exceeding their accumulation. This is based on the finding of low plasma and high urinary values for pitocinase in one case of eclampsia.

Of the 16 cases studied to date, only three had plasma pitocinase levels which fell within the normal range. Seven had values which were high, and six had values which were low for the corresponding period of pregnancy. There is no apparent correlation between the severity of the disease and the plasma pitocinase level. In the seven cases of eclampsia, for example, three values were high, one was normal, and three were very low. In two cases of pregnancy complicated by severe arteriolar hypertension, normal values were observed.

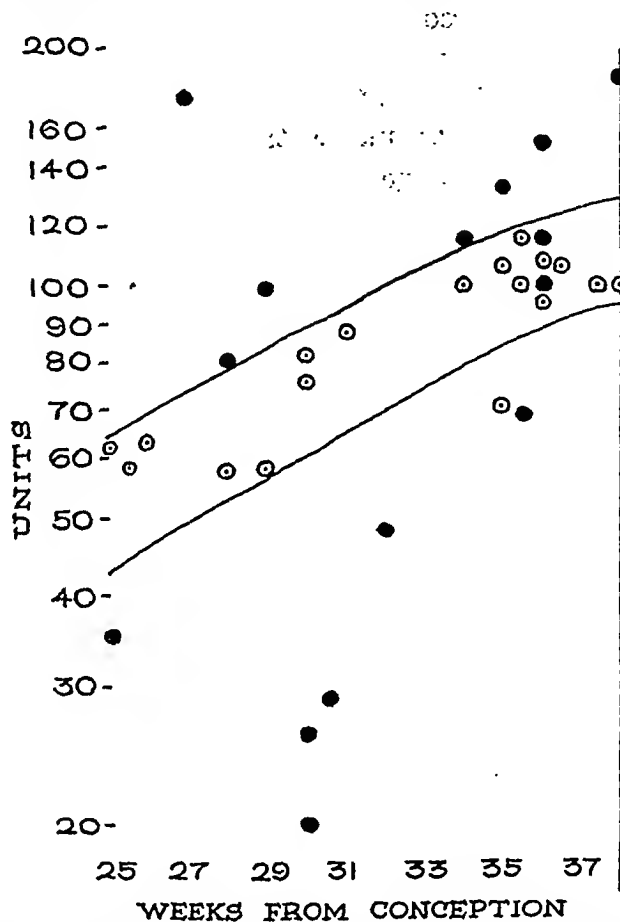


Fig. 3.—Plasma pitocinase levels in pre-eclampsia and eclampsia (solid circles), compared with the normal range for the last trimester (open circles).

### Discussion

It is interesting to compare these observations on pitocinase with the exhaustive studies which Ahlmark recently made on the histaminase activity of pregnancy plasma.<sup>16</sup> This latter enzyme, which is a diamine oxidase having no inactivating properties upon pitocin, nevertheless has a similar thousand fold increase during pregnancy. In contrast to pitocinase, the histaminolytic enzyme appears somewhat later and levels off sooner, but it demonstrates the same logarithmic increase during early pregnancy. Ahlmark claims that from the fifth to the fourteenth week after conception he can estimate the duration of pregnancy within six days. The method for plasma histaminase determination is somewhat more cumbersome than that for pitocinase, but it is already being used in Stockholm as a routine pregnancy test and as a prognostic aid in cases of threatened abortion.<sup>17</sup> In pre-eclampsia and eclampsia, plasma his-

test would be the examination of those species of animals in which the estrogen "spiegel" of the plasma during pregnancy resembles that of the human—for example, the mare.

These are admittedly only a few, and rather unimportant, suggestions prompted by Dr. Page's stimulating report. All must agree that he has done a workmanlike job of investigation and has made a real contribution. Its future development will be followed with great interest.

DR. CHARLES H. PECKHAM, JR., Hartford, Conn.—The theoretical aspects of Dr. Page's paper have been discussed by Dr. Bachman. I should like to make a few remarks concerning practical applications of this work which may develop in the future. First, it seems likely that the method may become somewhat commonly employed in diagnosing pregnancy. Most of the tests in use up to the present time carry with them a sufficient percentage of error as to leave a good deal to be desired. In Dr. Page's series there was one doubtful reaction, while the others were clearly positive or negative. Furthermore, the test is not a time-consuming one and, frequently in obstetrics, problems arise where time is the essence of diagnosis.

Before reading the paper, I hoped that it might produce something to add to our knowledge of the cause of the onset of labor. It is a matter of general agreement that the uterus in early pregnancy reacts very little to pitocin. The reaction increases as the pregnancy advances, and is greatest at about the time of the onset of labor. It is puzzling to find an enzyme in the plasma capable of inactivating pitocin, and particularly to find it in highest concentration at a time when the uterus is most sensitive to an oxytocic substance.

It is, furthermore, difficult to understand why an enzyme apparently elaborated by the placenta should take four weeks after the extrusion of this organ before it has entirely disappeared. Also, if we assume that the enzyme is a product of the placenta, why would not the concentration decrease as soon as the product of conception dies? Finally, placentas delivered after the estimated date of confinement frequently show evidences of senescence. One would suspect in these cases a decrease in plasma pitocinase, but such was not Dr. Page's findings.

The problem as to why the plasma pitocinase level was high in certain cases of toxemias and low in others deserves further investigation, particularly since there was no clinical differences found in the two groups. I believe the essayist should conduct follow-up studies on these patients in order to ascertain whether some of them developed permanent vascular damages while others did not.

DR. PAGE (Closing).—So far as the occurrence of pitocinase in closely related species are concerned, I have had no opportunities to obtain such material, but a pregnant monkey would be a welcome addition to my group of patients.

I failed to mention that when this method is used as a qualitative test for early pregnancies, the fresh plasma and pitocinase incubated *in vacuo* in a Thunberg tube, with a heavy layer of toluene on the surface, for eighteen hours. Of 20 additional tests on women who were less than eight weeks pregnant, all have been positive, while only traces (less than 0.05 units/ml. of plasma) have been found in nonpregnant subjects. We have not found a subject who suspected pregnancy in less than seventeen days after conception.

existence, but the week of pregnancy may be closely approximated. In true pre-eclampsia or eclampsia, the plasma levels are scattered on both sides of the normal range, indicating that an enzymatic disturbance is associated with this disease.

Appreciation is expressed for the able assistance of Mrs. Dean Rucker and Miss Eleanor Enos.

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### Discussion

DR. CARL BACHMAN, Philadelphia, Pa.—Dr. Page's careful quantitative study of the inactivation of posterior pituitary extracts by pregnancy plasma draws attention to a little-known sector of the field of enzyme physiology. I should therefore like to comment on a few of the theoretical, rather than the practical implications of his work.

His demonstration of the strikingly consistent and remarkable rise in concentration of "pitocinase" during pregnancy arrests attention as being a new contribution to our knowledge, and well worth further investigation. It would be interesting, for example, to know more about the nature and specificity of this enzyme. Dr. Page has indicated that it may be active against substances other than pitocin, and this, if true, would enhance its physiologic and clinical interest. Indeed, I think he is doing rather less than justice to his own good work by his coinage and use of a term having so narrow a meaning as "pitocinase."

It would also be interesting to know more about the site of formation or release of this enzyme during pregnancy. Dr. Page has suggested its probable production by the growing trophoblast, and this would seem to be its most likely source. However, one should bear in mind that a similar, and conceivably identical, enzyme is richly distributed intracellularly in several tissues, including the erythrocytes of men and nonpregnant, as well as pregnant, women. It is, therefore, at least theoretically possible for such a pre-formed intracellular enzyme to be released during pregnancy through altered conditions of cell permeability. In this connection the possible role of the sex steroids suggests itself, for it will be remembered that these steroids appear in plasma during pregnancy in a rising curve of concentration very strikingly comparable to that which Dr. Page has demonstrated for "pitocinase." Of course, the apparent absence of the enzyme in fetal plasma argues against the possibility suggested, unless it can be shown that the preformed enzyme is also absent in fetal tissues and erythrocytes. But the notion would bear examination, if only to enable us to have a firmer theoretical floor under the proposed use of this enzyme reaction as a specific diagnostic test of pregnancy. As "leads" it might be useful to test for the presence of the enzyme in such conditions as hemolytic ictero-anemia and obstructive jaundice. Another interesting



TABLE I. EFFECT OF CERVICAL MUCUS OF NORMAL WOMEN ON BACTERIA

ORGANISM	METHOD OF TESTING*	RESULTS†
<i>Streptococcus hemolyticus</i>	Plates streaked	50% showed inhibition
	Plates poured	63% showed inhibition
<i>Staphylococcus aureus</i>	Plates streaked	67% showed inhibition
	Plates poured	80% showed inhibition
<i>Neisseria gonorrhoeae</i>	Plates streaked	72% showed enhancement

\*Cervical mucus, in amounts ranging from 6.7 to 226 mg., was introduced into suspensions of 24-hour cultures of the organisms indicated. After two hours of incubation at 37° C., plates were poured or streaked.

†The colonies were counted after twenty-four hours' incubation and compared with counts made on the control cultures containing no cervical mucus. None of the resultant cultures of *Streptococcus* or *Staphylococcus* in media containing cervical mucus showed enhancement, and none of like cultures of *Neisseria gonorrhoeae* showed inhibition.

by the addition of cervical mucus to the culture medium, may add significance to the observed persistence for many months of gonorrheal infections in cervixes which remain otherwise fallow.

From their observations on cattle, Woodman and Hammond<sup>9</sup> regarded the liquefaction of mucus, such as occurs at estrus, as a requisite to the free progression of spermatozoa through the cervix. A gradient in electric potential of 3 to 5 millivolts between the zone of contact of cervical mucus (pH 9 to 9.6) and semen (pH 7 to 8) has been described by Miller and Kurzrok.<sup>10</sup> They suggest that this difference in potential may be a directing factor in the first orientation of spermatozoa in the female genital tract. Using in vitro methods, these same workers observed that when the mucus is infected, highly viscid, and opaque, the sperm in the proximity to it will not congregate at its boundary, nor will they try to penetrate the mass.

Séguy, in 1933,<sup>11, 12</sup> qualitatively described an increased amount of cervical mucus at the time of ovulation as determined by direct inspection of the ovaries. At this time the mucus was noted to be most translucent, acellular, and penetrable by spermatozoa. Similar qualitative results were reported by Lamar,<sup>13</sup> who introduced an improved technique for studying the penetration of cervical mucus by spermatozoa. Inasmuch as spermatozoa are ejaculated into an entirely new environment, and since their initial task is to overcome the obstacle of cervical mucus, the characteristics of this secretion at different times of the menstrual cycle appeared to be of sufficient importance to justify a quantitative in vitro study of factors which might assist or hinder the migration of spermatozoa through the cervical canal.

### Experimental

**Subjects.**—Young women, for the most part medical students or laboratory technicians, who were in good health, and who had normal menstrual cycles and normal pelvic findings, served as subjects in these studies. Basal temperature records of all these subjects showed a typical midcycle shift from a lower to a higher level. This, with collateral evidence, has been regarded as a sign of ovulation.

**Collection of Material.**—Cervical mucus was obtained throughout the cycle, save during menstruation, by aspiration from the external os and from the cervical canal. An effort was made to obtain all the mucus available at any one time. All specimens were weighed.

### Results

**Amount of Mucus.**—Although the production of mucus varies from cycle to cycle and from subject to subject, the monthly patterns are quite similar.

## CYCLIC CHANGES IN THE PHYSICAL AND CHEMICAL PROPERTIES OF CERVICAL MUCUS\*

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THE escape of a vaginal discharge, which rustic herdsmen have long regarded as a sign of estrus in their stock, finds its counterpart at midcycle in the human female. This discharge, which intelligent and observant women<sup>1</sup> and clinicians recognize as a second flux in the menstrual cycle, is traceable to the cervix.<sup>2</sup> While one may infer that this mucus normally contains increments from the uterus, it is not yet known to what extent the endometrium contributes to the character of the mucus which collects at the external os.

Rhythmic changes in the cervical glands with greatest development in the second half of the cycle have been described by Hartman<sup>3</sup> in the monkey, and by Wollner<sup>4</sup> in women. Sjövall,<sup>5</sup> however, noted that the proliferation reached its highest point at the time of ovulation, and thus gave a histologic explanation for the secretory changes, which can be observed directly by clinical examination. It is at the time of ovulation during the phase of maximal follicular development that the greatest yield of clear mucus may be obtained at the cervical os.<sup>6</sup> This finding has also been observed following supracervical hysterectomy. Since women upon whom bilateral oophorectomies and supracervical hysterectomies have been performed may be stimulated to the production of large amounts of clear mucus by the administration of estrogens, it seems established that the cervical glands are susceptible to or controlled by hormones.<sup>2</sup>

One may here join in with the speculations of others concerning certain functions of cervical mucus. On a priori grounds, one might attribute to it a protective function shared by the secretions of other mucous surfaces. By its replenishment, it may well aid in the removal of foreign bodies, cellular debris, and bacteria enmeshed in its substance. DeLee<sup>7</sup> regarded the mucus as presenting a barrier to the uterus against infection, a view again expressed by Goodall in 1945.<sup>8</sup> However, the evidence as to how the mucus exercises this property, apart from its action as a physical obstruction, has to my knowledge not been adducted.

The current interest in antibiotics stimulated an investigation now in progress by a colleague, Dr. Charles Carpenter. The data now on hand suggest that cervical mucus, in vitro, may inhibit the growth of certain strains of *Streptococcus hemolyticus* and *Staphylococcus aureus*, and enhance the growth of certain strains of *Neisseria gonorrhoeae* (Table I). This latter finding, i.e., the apparent encouragement to the growth of *N. gonorrhoeae*, given

\*Read (by invitation) at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

progressively worsened and the patient died on the fifteenth postpartum day despite energetic chemotherapy. Blood culture revealed hemolytic streptococci; autopsy showed generalized peritonitis and acute endocarditis.

CASE 10.—(38-24611.) R. H., aged 40 years, para vi, gravida vi, was admitted July 26, 1938, at term. After artificial rupture of membranes and a latent period of twenty-four hours, a 3,218-gram living infant was delivered spontaneously following a short labor. One hour prior to delivery a chill and temperature of 101.8° F. appeared. Shock, anuria, cyanosis, sepsis, and delirium followed delivery and death occurred on the thirteenth postpartum day. Blood cultures were negative. No autopsy was granted.

CASE 11.—(38-29937.) B. W., aged 34 years, para viii, gravida ix, was admitted in coma on Oct. 25, 1938, approximately seven months pregnant. Four convulsions and hematuria had been noted prior to admission. Labor commenced spontaneously and a 2,375-gram stillborn infant was delivered spontaneously after a short labor. Coma, pulmonary edema, and fever (105° F.) persisted, and death resulted forty-eight hours after delivery. Autopsy was refused.

CASE 12.—(39-7131.) E. L., aged 17 years, para 0, gravida i, was admitted with latent syphilis on June 9, 1939, approximately eight months pregnant. Following the tenth dose of neoarsphenamine, nausea, vomiting, and fever (101.4° F.) developed. A 2,420-gram living infant was delivered spontaneously after a short labor. Cough, hemoptysis, fever (105.6° F.), and leucopenia developed and death occurred on the first postpartum day in spite of energetic treatment. Hemolytic staphylococci were recovered from sputum and blood. Autopsy disclosed acute pulmonary edema, lobular pneumonia, hemolytic staphylococcus aureus septicemia and agranulocytosis.

CASE 13.—(38-18243.) R. S., aged 21 years, para ii, gravida iii, was admitted on May 27, 1940, at term. After artificial rupture of the membranes a transverse presentation developed which external manipulation failed to correct. Following this, the fetal heart sounds disappeared, and the temperature reached 101.6° F. After fifty hours of labor a 3,765-gram stillborn infant was delivered by cesarean hysterectomy. Cough, abdominal distention, fever (104.4° F.) and delirium developed during the puerperium, and death occurred on the tenth postoperative day. Beta hemolytic streptococci were recovered from the cervix, although blood cultures were negative. No autopsy was granted. Microscopic sections of the uterus showed no infection.

CASE 14.—(41-1862.) E. G., aged 20 years, para 0, gravida i, was admitted in coma on Feb. 8, 1941, approximately nine months pregnant. Six convulsions had occurred prior to admission. Examination disclosed a temperature of 100.4° F., four-plus albuminuria, and blood pressure of 220/106. After artificial rupture of the membranes and a short labor, a 2,800-gram stillborn infant was extracted (breech). Coma, fever, and convulsions persisted, and death occurred on the first postpartum day. Autopsy showed pulmonary congestion and edema, pleural effusion, and peripheral necrosis of the liver.

CASE 15.—(40-3592.) M. G., aged 27 years, para v, gravida ix, was admitted on Aug. 29, 1941, with vaginal bleeding at term in labor. The admission temperature was 102.3° F. A 3,500-gram stillborn infant was delivered spontaneously after a short labor. Bleeding and shock followed delivery. After supportive transfusions and a uterine pack failed to control hemorrhage, subtotal hysterectomy was performed ten hours after delivery. Death occurred on the first postoperative day. No autopsy was granted. Microscopic sections of the uterus disclosed acute suppurative endo- and myometritis and examination of placenta supported the clinical impression of placenta previa.

When the amounts of mucus obtained are plotted on a scattergraph, one notes that the maximal production occurs on about the fourteenth day of the usual 28-day cycle. A fairly abrupt rise in the amount of mucus is noted before the fourteenth day, and a sharp fall afterwards. At the time of the peak production, a ten- to twelvefold increase is noted over the 20 to 60 mg. quantity present in the postmenstrual and premenstrual periods.

In these studies, it was observed that a time relationship exists between mucus production and the basal temperature shift.<sup>6</sup> The maximal secretion is noted to occur in the two-day period during which the rise in the basal temperature takes place. Gross tests also indicated that the viscosity of the mucus is lowest at this time of greatest output, a phenomenon described qualitatively by Séguy<sup>11, 12</sup> and Lamar.<sup>13</sup>

*Viscosity.*—Cervical mucus as it collects at the external os is not homogeneous and does not behave as a true fluid. Such complex properties as density, surface tension, tackiness, film formation, and dispersibility influence its fluidity. Possible admixture with endometrial secretions and contact with the vaginal acidity and flora may well alter its flow characteristics. However, by using an objective method for measuring the fluidity,<sup>14</sup> one finds that the resistance to flow of mucus through a capillary tube, expressed as viscosity, decreases as one approaches the midcycle. The lowest viscosity, though variable over a period of a very few days, occurs at the time of ovulation coincident with the shift of the basal temperature. At this time the output of mucus is greatest. Mucus which requires as much as 100 seconds to traverse a given distance through a capillary tube, a condition typical of the postmenstrual and premenstrual periods, is replaced at midcycle by a thin watery secretion having such fluidity that only 2 to 3 seconds are required for it to negotiate the same distance under the same set of standard experimental conditions.

*Penetrability of Mucus by Spermatozoa.*—When the fluidity of mucus, expressed as the converse of the viscosity, and the penetrability of mucus by spermatozoa are graphically compared, a high degree of correlation is noted.<sup>14</sup> At midcycle, when the mucus possesses its lowest viscosity, spermatozoa may travel through it at the rate of 3 mm. or more per minute. Before and after the ovulatory phase, their progress through the mucus may be reduced to less than 0.25 mm. per minute; in fact, at times the attempts of the spermatozoa to negotiate the mucus barrier fail entirely.

*Water Content.*—The fluidity of mucus at midcycle suggested that its water content is greatest at this time. By test it was determined that the water content of cervical mucus ranges from 92 to 94 per cent in the postovulatory and preovulatory phases. This low figure may be due to the high cellular content. At midcycle, as indicated by the thermal sign of ovulation, the water content rises to 97 to 98 per cent. This fact might of itself help to explain the increased penetrability of mucus by spermatozoa at this time (Fig. 1).

The copious outpouring of mucus at midcycle, in contradistinction to the menstrual flow, appears to involve but little cell destruction and loss, since the secretion at this time is translucent and relatively acellular. It has not been possible to do actual cell counts because of the difficulty of effecting satisfactory dispersal of the mucus with its enmeshed cells over a grille. During the phase of low output the mucus is viscid, opalescent, or even turbid. These turbid or opalescent specimens, on microscopic examination, are found to be very rich in cells and debris.

*Chemical Content.*—MacLeod<sup>15, 16</sup> made the significant observation that the metabolism of human spermatozoa suspended in Ringer-glucose solution is largely glycolytic, and that aerobic glycolysis amounts to about 80 per cent

of the anaerobic. Substrates containing such utilizable sugars as glucose, maltose, mannose, fructose, and glycogen were found to be essential for the maintenance of glycolysis and prolonged activity of the spermatozoa.

Since sugar is such an important factor in the metabolism of human spermatozoa, it is but natural that it should be supplied by the ejaculate. Huggins and Johnson<sup>17</sup> demonstrated that the glucose content of semen, which averages about 300 mg. per cent,<sup>17, 19, 20</sup> is derived from the seminal vesicles. MacLeod<sup>18</sup> has shown that 75 per cent of the spermatozoa are present in the first 40 per cent of the normal ejaculate. McCarthy<sup>19</sup> has shown that incubation for twenty-four hours reduces the glucose content of semen to 10 to 25 per cent of the original level.

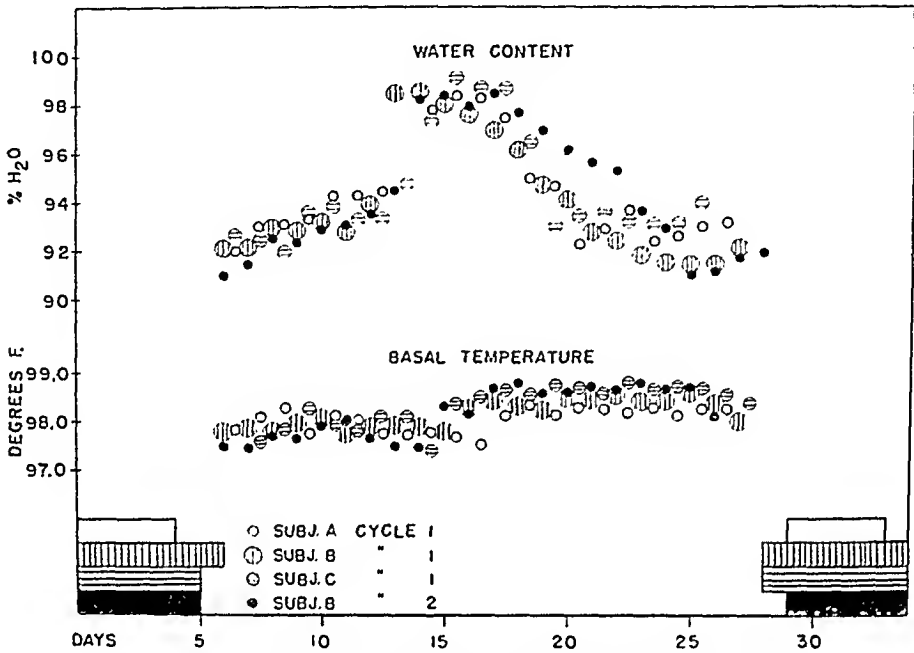


Fig. 1.—The increase in water content of cervical mucus at the time of ovulation as indicated by the shift in basal temperature. Three subjects; four cycles.

Hughes<sup>21</sup> and Novak<sup>22</sup> have recently called attention to the important part played by glycogen in the nutrition of the egg before and after fertilization, and also after nidation. As though to anticipate this requirement, the genital tract is generously supplied with this carbohydrate. Since the sperm cells on penetrating cervical mucus carry with them no substantial reservoir of sugar, MacLeod<sup>23</sup> has hypothesized that in all probability they find a suitable substrate in the female genital tract to maintain their motility. This suggestion led to an investigation in our laboratory of the carbohydrates in cervical mucus.

The cycle, exclusive of the menstrual period, has been divided arbitrarily into three phases: preovulatory, ovulatory, and postovulatory, the ovulatory period corresponding to those days during midcycle on which the amount of mucus is markedly increased. The daily results have been averaged according to the phase of the cycle (Table II). The Somogyi modification<sup>24</sup> of the Shaffer-Hartman copper reagent has been used for the determination of the amount of reducing substance present.

When mucus is added to the copper reagent, it is found to contain a small amount of free reducing substance. Whether this reducing substance is actually a carbohydrate is not yet known.

If a weak iodine solution is added directly to the mucus, mahogany colored mottling and streaks are seen, a reaction indicating the presence of

TABLE II. CONCENTRATION OF REDUCING SUBSTANCES IN CERVICAL MUCUS

	PREOVULATORY PHASE		OVULATORY PHASE		POSTOVULATORY PHASE	
	(% GLUCOSE)		(% GLUCOSE)		(% GLUCOSE)	
<i>Free Reducing Substances</i> (4 cycles)						
Draining	0.11		0.05		0.12	
Canal	0.09		0.04		0.16	
<i>Glycogen Precipitation Method</i>						
1. Free reducing substance in precipitate						
Draining	0.02		0.01		0.03	
Canal	0.00		0.00		0.00	
2. Free reducing substance in supernatant						
Draining	0.08		0.06		0.15	
Canal	0.08		0.03		---	
3. Acid hydrolysis of pre- cipitate (6 cycles)						
Draining	0.32		0.23		0.27	
Canal	0.15		0.05		0.20	
4. Acid hydrolysis of precip- itate and supernatant of same mucus specimen						
	ppt.	super.	ppt.	super.	ppt.	super.
Draining	0.38	0.24	0.19	0.20	0.60	0.16
Canal	0.19	0.28	0.10	0.14	0.14	0.14
<i>Direct Hydrolysis</i> (5 cycles)						
Draining	0.55		0.41		0.79	
Canal	0.60		0.31		0.83	

glycogen. When the mucus is dissolved in strong alkali followed by the addition of 95 per cent alcohol, a standard procedure for the determination of glycogen, a precipitate is thrown down which also gives the characteristic color reaction with iodine. This precipitate contains little, if any, free reducing substance, but after acid hydrolysis measureable quantities of reducing substances can be determined. If the precipitate is glycogen, glucose should be formed on hydrolysis; preliminary fermentation studies show that approximately 60 per cent of this hydrolytic product is fermentable. The supernatant obtained from the treatment of cervical mucus with strong alkali followed by the addition of alcohol contains amounts of free reducing substance comparable to those found in untreated mucus, and acid hydrolysis of this supernatant solution yields even larger quantities of copper reducing substances.

Acid hydrolysis of the mucus itself yields larger amounts of reducing substances than by any of the methods previously mentioned. Direct hydrolysis would, of course, measure all the reducing substance that mucus might contain. From the data at hand, there appears to be a cyclic variation in the amount of fermentable sugars following direct hydrolysis. In the preovulatory phase, 48.7 per cent of the glucose concentration was fermentable, 28.7 per cent in the ovulatory phase, and 49.8 per cent in the postovulatory phase.

In all of the carbohydrate studies a cyclic variation in the concentration of the reducing substance is noted, with the lowest concentration occurring during the ovulatory phase. This fact would appear to be correlated with the acellularity characteristic of this period of the cycle.

Since the amount of reducing substance obtained by direct hydrolysis is greater than the sum of that obtained from the untreated mucus plus that obtained by hydrolysis of the glycogen precipitate, the presence in the mucus of reducing substances other than carbohydrate was sought. Hewitt<sup>25</sup> found that tyrosine had approximately the same reducing power as dextrose, and

TABLE III. COLOR REACTIONS GIVEN BY CERVICAL MUCUS

NAME OF TEST	REACTION PRESUMABLY DUE TO PRESENCE OF
1. Iodine test	Glycogen
2. Biuret reaction	Peptide linkage
3. Millon's reaction	Hydroxy-phenyl group, as in tyrosine
4. Liebermann's reaction	Condensation of trypto- phane with an aldehyde or other carbonyl group
5. Xanthoproteic reaction	Phenyl group, as in phen- ylalanine, tryptophane, and tyrosine
6. Sulfur test	Unoxidized sulfur, as in cystine

NOTE: These reactions were obtained on both draining and canal specimens. The color reactions given by mucus obtained during the ovulatory phase were usually fainter than those given by samples obtained during the pre- and postovulatory phases.

tryptophane about 80 per cent as much. In his work he used the Hagedorn-Jensen reagent, which is slightly more sensitive than copper reagents to reduction by noncarbohydrate compounds. In the belief that certain amino acids may account for some of the reduction of the copper reagent, tests for their presence were made on the mucus. Color reactions were obtained that are characteristic of the peptide linkage; the hydroxy-phenyl group, as in tyrosine; the condensation of tryptophane with an aldehyde or other carbonyl group; the phenyl group, as in phenylalanine, tryptophane, and tyrosine; and unoxidized sulfur, as in cystine (Table III). The color reactions were usually fainter in the ovulatory phase than in the preovulatory and postovulatory phases. This fact is probably due to the acellularity and high water content of the mucus at this time.

The presence of amino acids in cervical mucus is strongly suggested by these color reactions. What their significance may be is not established. One may here offer the presumption that they share with carbohydrate the function of nutrition of the gametes, and perhaps also of the fertilized egg.

### Summary

Cervical mucus at midcycle is increased in amount, acellularity, water content, and fluidity. Furthermore, cervical mucus at this time is well supplied with carbohydrate and presumably amino acids. From a teleologic standpoint, we may conclude that because of these characteristics the sperm, on deposition in the vagina, find an environment propitious for their nutrition and migration through the cervical canal.

The author wishes to acknowledge the very able assistance and cooperation of his associate, Dr. Ellenmae Viergiver, in the prosecution of this study. This investigation has been aided by a grant from the Ortho Research Foundation.

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### Discussion

DR. JOHN ROCK, Brookline, Mass.—Dr. Pommerenke and his colleagues are developing for us factual standards and actual measurements. The uterus is a highly differentiated organ, good for only one thing, reproduction. The egg gets in at one end and, in spite of the fact that Pineus has already been able to start rabbit eggs on their way to growth by the use of only heat or salt, spermatozoa must enter the other end to fertilize the human egg. In order to reach it, they must have a proper medium, and Dr. Pommerenke has limited his discussion to the fluid in one small segment of the uterus.

I approve of the term "ovulatory phase." We hear much about the variation in the amount and the quality of mucus through the menstrual cycle. There is a short period at first when it is scanty. Then comes the ovulatory phase, at some time in which ovulation takes place, and during which mucus is plentiful. Tests for ovulation indicate, I believe, an ovulatory phase, and not necessarily the moment of ovulation.

The fluid in the cervix, as has been said, may be very profuse. Frequently patients complain of leucorrhea, which is not necessarily pathologic, but merely the result of hyperfunction of normal glands. The condition is usually limited to about a week and does not necessarily require treatment. However, sometimes this discharge is so profuse as to merit attention. Nevertheless, it would be a great mistake so thoroughly to treat the cervix by diathermy as to relieve the patient's complaint, and yet leave the cervix so dry that spermatozoa could not make progress through it.

Dr. Pommerenke's report of Dr. Carpenter's demonstration of the bactericidal property of cervical mucus at ovulation time is very interesting. Perhaps it explains how uncommon it is for the millions of sperm to infect the susceptible tube through which they travel after leaving semen that is often highly contaminated. But the gonococcus does get into the tube. Do the sperm carry it through the mucus which in vitro favors its growth?

Dr. Pommerenke has pointed out various qualities of this mucus which possibly serve the purposes of sperm. Such investigative work is bound to be of great practical value in the control of conception, having in mind, of course, the positive rather than the negative aspects of this high function.

The time factors are interesting. The egg is probably susceptible to fertilization for only a matter of perhaps twelve to forty-eight hours after its release from the follicle. Spermatozoa are functional for probably forty-eight hours. It takes the good ones only three to four hours to travel from the vagina to the ampulla of the tube. Where do they get the energy to do this? MacLeod has shown that sperm in vitro live longer and are progressively motile longer if their medium contains some easily utilizable sugar. But during the ovulatory phase, Dr. Pommerenke finds that the concentration of reducing substances like glucose is less than at other times. The fluid of the ejaculate is high in carbohydrate, but sperm are in this for only a short time. Nor can there be much for them in the uterine fluid, since glycogen does not appear in appreciable amounts in the



endometrial glands until after ovulation. Perhaps, though they can use carbohydrate, good ones do not need much, if any. Three times pregnancy has been established in hitherto barren women after injecting into the uterus a twice-washed suspension of husband's spermatozoa in Ringers-Locke's solution that contains only 0.1 per cent of dextrose. It is conceivable and worthy of contemplation that the varying carbohydrate content of the cervical and uterine fluid, together with other chemical constituents and physical qualities, may have more direct reference to phylogeny than to physiology. They may be inherited factors passed down from long distant ancestors, in whom they were physiologically useful, to much differentiated humans in whom they persist but have no function. Whether or not this is so can only be determined by studies similar to those of Dr. Pommerenke.

DR. ISIDOR C. RUBIN, New York, N. Y.—The secretion of cervical mucus under normal and pathologic conditions, its physical and chemical composition and properties, and its specific purposes are matters which have been dealt with in a more or less desultory manner in the past. This has not been due to lack of interest so much as to the difficulties involved in the technical study of cervical mucus. One of the chief reasons for active revival of interest in this subject has been the importance of bringing relief to childless married couples who increasingly enlist sympathetic medical advice to enable them to have children. Dr. Pommerenke's paper is therefore welcome as a serious attempt to solve theoretical questions concerning cervical mucus.

That there are cyclic changes in the cervical secretion may be accepted both on the basis of the new evidence presented by Dr. Pommerenke and numerous clinical and histologic observations. A hormonal relationship between ovarian function and the secretion of cervical mucus has been held for a long time; and cervical erosion has also been suspected of being the result of dysfunction of the ovaries.

We have struggled with this question for some years at Mount Sinai Hospital and had planned to attack the problem somewhat along the same lines as those of Dr. Franklin Hollander of the Department of Physiology, who has done much work on gastric and intestinal mucus. But with the intervention of the war which brought on difficulties in getting needed apparatus, together with the shortage of man power, we had to abandon the full program.

Evidently Dr. Pommerenke was able to solve the matter of getting the specimens of mucus in sufficient quantities upon which to make determinations. We aspirated the cervical canal under varying degrees of pressure up to 20 pounds in some cases, and in others we applied cellulose or aluminum caps to the cervix for several hours. In normal cases we were not able by aspiration to get enough mucus for the tests we had planned. The pathologic cases gave us more mucus but, after aspirating it into a pipette with an expanded collecting chamber, it was difficult to remove the specimen for testing. This was later solved by devising a sort of trap-door collecting chamber with removable parts. In obtaining the pH of the cervical mucus in situ, difficulties were encountered because we had no suitable electrode and could not have one constructed.

Concerning the behavior of spermatozoa in cervical mucus, a few observations with the Hühner test and artificial insemination may be mentioned. There have been instances where spermatozoa remained motile after one or two hours in the vaginal secretion, although the spermatozoa found in the cervical secretion were nonmotile. The cervical mucus under such circumstances was not necessarily viscid or grossly altered. In most cases it was scanty. As a rule, motility was observed in the cervical mucus, while the sperm in the vaginal secretion were nonmotile. In some cases spermatozoa have been found to remain actively motile in thick mucus-pus for a longer time than in the vaginal secretion.

The predominant number of oval or olive-shape heads of the spermatozoa in the cervical secretions in contrast to the spear or pear-shape heads of the spermatozoa found in the vaginal secretions and in the fresh unmixed ejaculate is a phenomenon not yet explained. Does the sperm head change on account of some physico-chemical property of cervical mucus which causes it to swell, or does the cervical mucus select these sperma-

tozoa out of the millions that make their way into the cervical canal, i.e., are there particular gametes present in the ejaculate in a certain percentage which find their way into the cervical canal? When semen containing spermatozoa with predominantly spear-shaped heads was mixed with cervical mucus, practically all the heads assumed the olive shape. This observation was made many years ago and subsequent observations have corroborated it.

The question of what constitutes endocervicitis clinically is another pertinent point of interest. Endocervicitis characterized by profuse mucopurulent discharge from the cervix and a high content of pus cells may be cleared up by the newer sulfonamide chemotherapy which, at the same time, demonstrates its infective nature. But there are many variations in the amount of cervical mucus and in the numbers of pus cells which may be found at all times of the menstruation-ovulation cycle. Are these findings analogous to those in the vaginal smear during the menstruation-ovulation cycle or shall we designate them as mild or moderate endocervicitis? Should it be found on the basis of a larger number of cases that mucus secretion is more abundant, containing no pus cells, and that it is less viscid on the fourteenth day of the menstrual cycle, it may be advanced as additional indirect evidence of ovulation, although it may prove eventually not to have such specific significance. Dr. Pommerenke apparently takes it for granted that the cyclical diphasic change in temperature is pathognomonic.

I think a point which should be borne in mind in connection with this discussion is that there is a marked difference between normal fertile couples and sterile matings. In sterility, resort to coitus during the so-called favorable period has been highly disappointing. There are undoubtedly other physical and chemical properties of the cervical mucus besides mucin and fluidity which favor, or militate against, penetrability and motility of spermatozoa. Whether they are immunologic in nature remains for the future to disclose.

Such investigation is especially tedious and requires the devotional cooperation of the young women submitting to the frequent examinations. Only the keenest interest and enterprise in prosecuting this particular work can yield data such as Dr. Pommerenke has been able to present. There is great need for more work of this kind. I should like to ask him in closing to describe some of the essentials of the technique for the guidance of others who may be similarly interested.

DR. POMMERENKE (Closing).—When the cervical secretion is scant it is almost always highly cellular. This can be demonstrated by microscopic examination when a great deal of cellular debris can be demonstrated.

As regards technique, the dry speculum is inserted into the vagina exposing the cervix. The mucus adhering to the surface is wiped away to prevent contamination of the specimens which are removed with a pipette attached to a suction syringe. One may ask how you got the mucus out of the pipette? This may be quite a job. Clean pipettes containing the secretion are emptied into test tubes and rinsings added. At times only about 20 mg. of secretion can be obtained. A high percentage of this is water. Microchemical methods are available for studying even such minute quantities of material.

## GRAPHIC PORTRAYAL OF RELATIVE PELVIC SIZE\*

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TWO general classifications of the bony pelvis exist, the etiologic and morphologic. The first, based upon manual mensuration, defines limits of normality of inlet size according to Litzmann, and of the outlet according to Williams, but disregards the midpelvis. The latter, developed by Caldwell and Moloy, is based upon the roentgenologic determination of pelvic shape and its effect upon the course of labor, but offers no criteria of size. Both classifications are complicated, and neither is of practical value to the medical student, general practitioner, or average obstetric specialist. There is need for a simple method of evaluation of pelvic adequacy. The purpose of this paper is to offer a visual method of depicting three essential pelvic planes in contrast with established norms. Results obtained from application of this method will be presented in a forthcoming communication.

The obvious method of evaluating size and shape of any passageway is to measure the length and breadth of each of a sufficient number of cross sections. Graphic reproduction of each cross section, especially when plotted on a sheet of paper in comparison with established norms, offers a clear and a visual conception of variations of contour. Since the total height of the bony pelvic cavity measures approximately 5 cm anteriorly and 10 cm. posteriorly, it is obvious that graphic portrayal of but three cross sections will provide sufficient knowledge of contour. Moreover, since bony dystocia of serious nature occurs most often at the inlet, less commonly at the midplane, and rarely at the outlet, these three pelvic levels were chosen for graphic portrayal. The contour of each plane can be sketched with reasonable faithfulness from knowledge of its anteroposterior and transverse diameters, and the point where they intersect. Admittedly, this method does not permit reproduction of the *exact* outline of each plane, and may not satisfy serious students of pelvic morphology, but the resulting diagram is sufficiently true to permit accurate prognostication of the course of labor.

In order to diagram each of the three pelvic levels, a normal gynecoid pelvis was selected and the outline of each level accurately obtained by shaping lead wire to its anatomic contours. The resulting shapes were corrected for minor variations and adjusted to accepted pelvic measurements. Ideal shape and size of the inlet, mid-, and outlet planes of an average, normal pelvis on a life-size scale were, therefore, accurately reproduced on paper. In addition, a centimeter scale was incorporated directly in the anteroposterior and trans-

\*Read at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

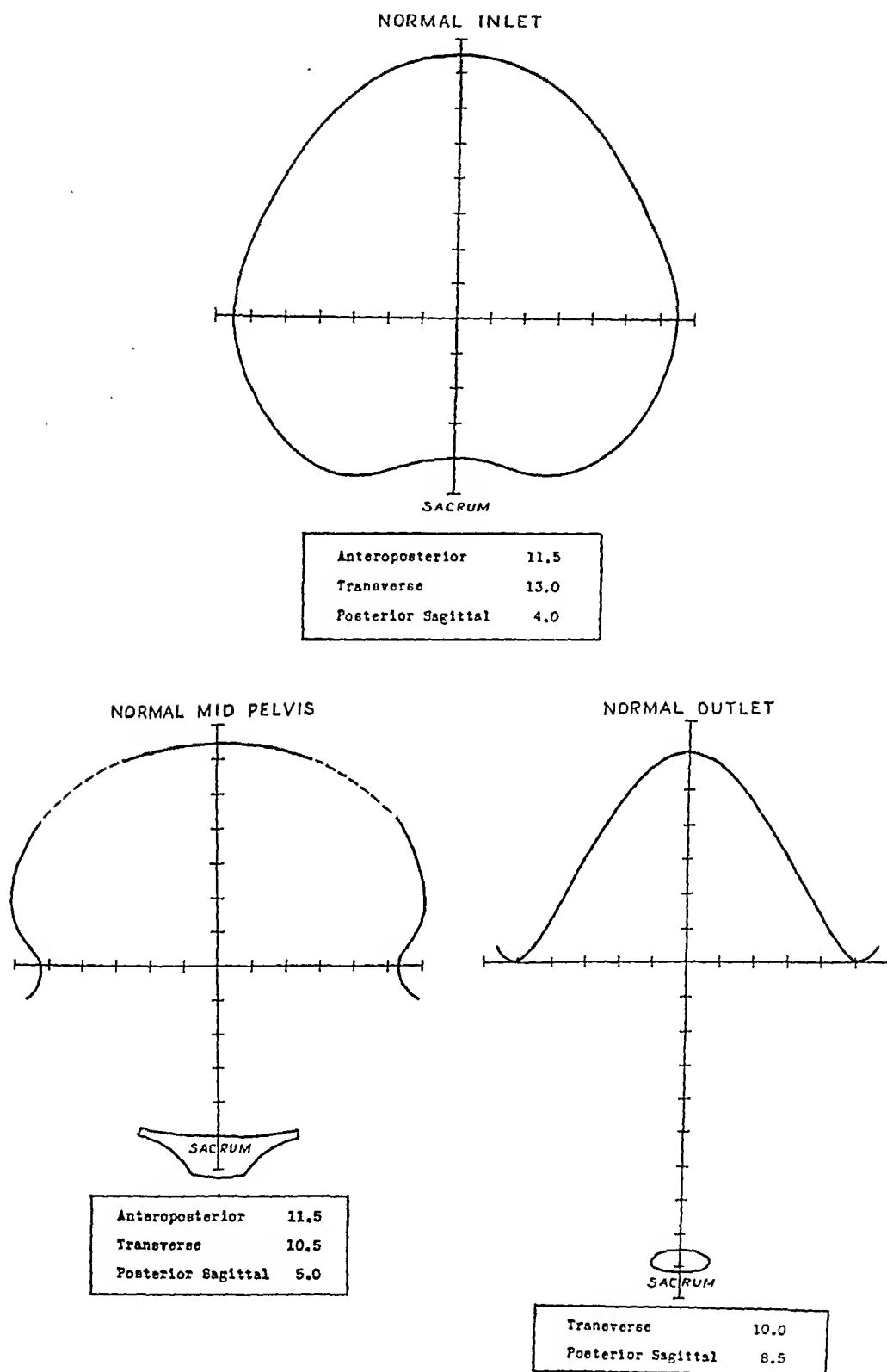


Fig. 1.—A—inlet, B—mid, and C—outlet planes of a normal gynecoid pelvis. The diagrams were obtained by shaping lead wire to the anatomic contours of the pelvis, correcting for minor variations, and adjusting to accepted pelvic measurements. The scale is in centimeters.

NOTE: All illustrations are reduced to the same size for the sake of ready comparison.

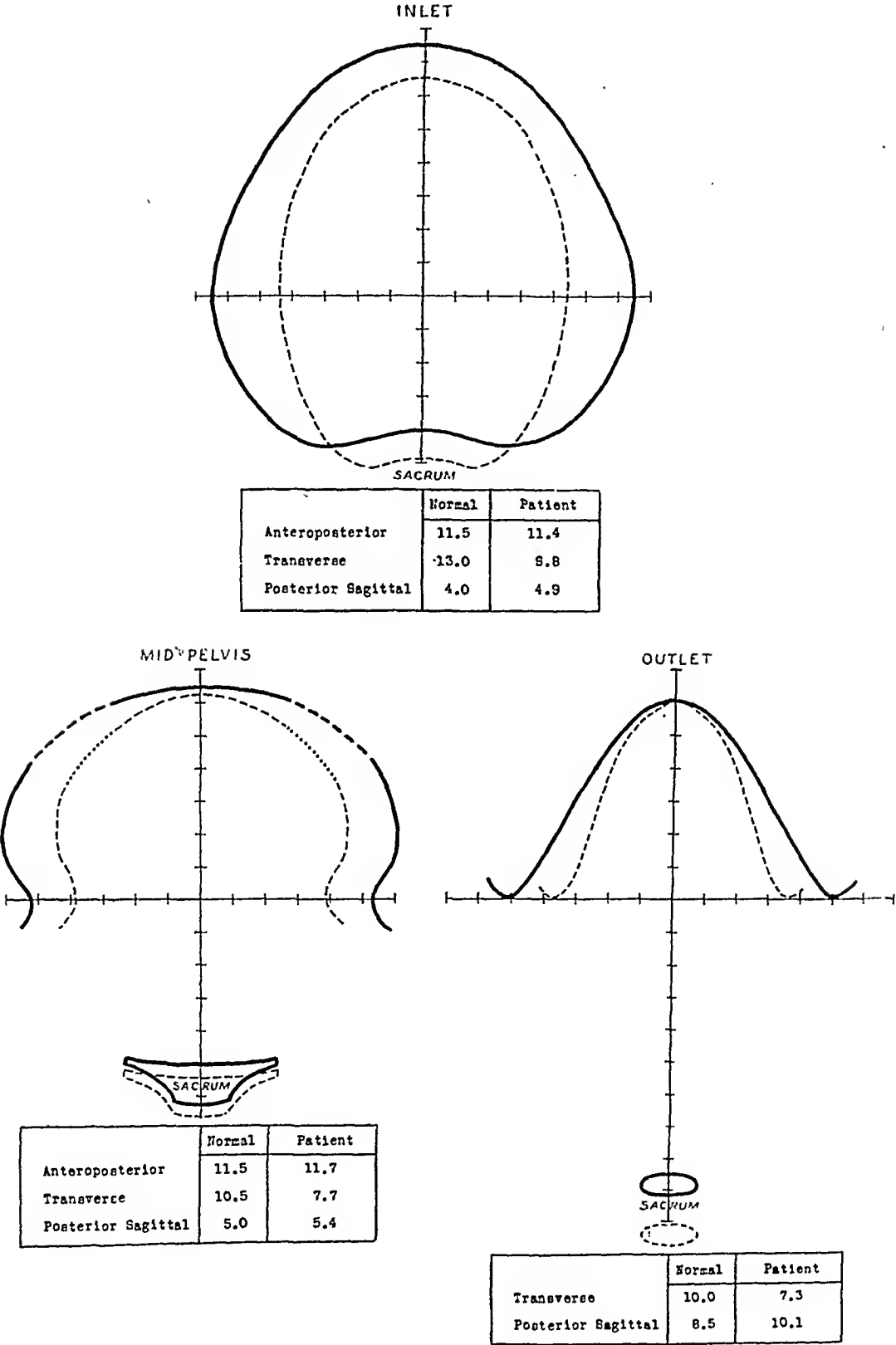


Fig. 2.—The dotted lines represent graphically an anthropoid type of pelvis of patient M. J. She was delivered by elective cesarean section because it was felt the head would not pass the midplane.

### Summary

Fever during labor may be due to dehydration, extragenital disease, or birth canal infection. The last is diagnosed by excluding the other two, or by the discharge of foul material from the tract. The primary lesion in infections of the genital tract is an amnionitis (placentitis) which subjects both the mother and the child to serious sequelae. In the mother, puerperal infection frequently develops and may be fatal, while aspiration pneumonia and septicemia by direct extension into the placental vessels constitute the chief risks to the child. In this series of 187 febrile labors, 129 presented evidence of birth canal infection alone or in combination with an extragenital factor. In the latter group, eight mothers and sixty-one infants died, mortality rates of 6.2 per cent and 46.9 per cent, respectively. Dehydration fever was followed by no maternal or fetal deaths, but pyrexia of extragenital origin (no evidence of uterine infection) led to a maternal death rate of 36.8 per cent and a fetal mortality rate of 42.2 per cent.

Treatment of dehydration fever and of extragenital diseases followed usual lines. On the other hand, therapy of intrapartum birth canal infections has been significantly and favorably altered by recognition of the dangers involved and by the use of the newer antibiotics, the sulfonamides, and penicillin, prophylactically and curatively.

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single piece of transparent plastic further simplifies the apparatus. Predetermination of fetal size is difficult and inaccurate, even with present roentgenologic methods of fetal cephalometry. Nevertheless, this plastic, cephalic cutout has proved its practical value. Generally speaking, when a given sized cephalic outline can be fitted exactly into the pelvic diagram, it may be concluded from a clinical standpoint that a child of equivalent size plus 500 Gm. can pass through the patient's pelvis. The 500 Gm. excess is probably accounted for by the process of molding.

With graphic portrayal of pelvic size and approximate shape in direct contrast with the normal, and by use of plastic cephalic cut-outs, it has been possible to make accurate prognostications of the course of labor. For example: A 29-year-old primigravida, at term, hospital number W-27796, was admitted Aug. 19, 1945, in labor, but with a floating head. Graphic representation of the pelvis revealed generalized contraction of inlet and midplane (Figs. 4-A, B and C). The child was estimated to be average in size. It was predicted the head would engage transversely, arrest at midpelvis, and that forceps rotation to obliquely anterior with extraction would be necessary, since the head could not traverse the midplane either in occipitoanterior or occipitotransverse position. This is precisely what happened. After a total labor of 32 and one-fourth hours, with a second stage of three and three-fourth hours, the head was arrested in left occipitotransverse position just above the ischial spines. Kjelland forceps were applied. The operator could not rotate at the level of arrest, and could not produce descent without rotation. By combination of both, he was able to bring the head through the mid-pelvis obliquely anterior, with subsequent easy extraction. The child weighed 3,692 Gm., and was gaining weight at the time of discharge.

Recapitulating, knowledge of six pelvic diameters will give all practical information necessary for evaluation of pelvic capacity. These diameters are the anteroposterior and transverse of the inlet and midplane, and the posterior sagittal and transverse of the outlet. Four of the six measurements can be obtained or closely estimated manually: the anteroposterior of the inlet; the transverse and posterior sagittal of the outlet; and the transverse of the midplane. Two pelvic measurements, the transverse of the inlet and the anteroposterior of the midplane, are measured in the living by roentgenographic means. From a practical standpoint, the transverse diameter of the midplane is commonly measured roentgenographically, although in 1930 Hanson described an instrument for its manual mensuration.

Ordinary roentgenograms are worthless in the evaluation of pelvic size, because the rays emanating from the tube target are not parallel and, therefore, enlarge the image. The enlargement is inconstant and depends upon the distance of the x-ray film from the object and from the target. Some form of correction is essential to determine size. Any acceptable roentgenologic technique will supply the measurements needed for graphic portrayal of pelvic planes. However, the methods generally employed are technically difficult and complex. Snow introduced a much simplified method of roentgenographic mensuration in 1940, based on geometric principles and employing a specially devised slide rule. In both conception and practice, it is within the capabil-

verse diameters. In practice, the outline of each plane is sketched on the basic diagram of its normal counterpart. Obviously, it is necessary to know where the two diameters intersect. The transverse diameter is exactly bisected by the anteroposterior unless there is unilateral pelvic distortion. On the other hand, the point at which the transverse diameter crosses the anteroposterior of each of the three planes is variable and must be determined by measurement of the posterior sagittal diameter. This can be accomplished for the inlet and midplane only by roentgenographic means. The technique of manual measurement of the posterior sagittal of the outlet is familiar to every obstetrician.

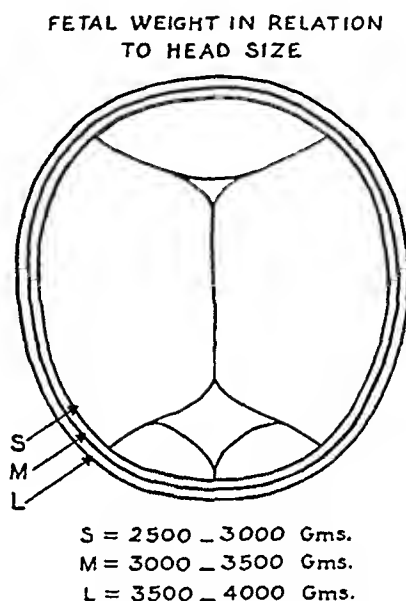


Fig. 3.—Fetal head diagram. In practice, this is made of a 2-mm. thick piece of transparent plastic, shaped to the contour of the largest size. The other two outlines are etched into the plastic.

Inlet contour (Fig. 1-A) is familiar from frequent portrayal, but the midplane is seldom illustrated (Fig. 1-B). Cross section diagrams of the outlet cannot be made, since there are two triangles in different planes, but with a common base. For the sake of completeness, however, both triangles may be projected as a plane (Fig. 1-C). The graphic depiction of a distorted pelvis in immediate contrast with the normal is so vivid that an assistant resident obstetrician said, "Now we are able to *see* the patient's pelvis!" The vividness of mental impression is exemplified by the following patient (Figs. 2-A, B, and C). This is a typical anthropoid pelvis and it seemed obvious that vaginal birth of a living, term-sized child would be difficult or impossible, especially with regard to the midplane. An elective cesarean section resulted in the birth of a 2,528 Gm. living child.

Decision concerning management of any given patient is greatly facilitated by applying a diagrammatic, transparent, plastic cutout of small, average, and large fetal heads to the graphic, pelvic diagrams (Fig. 3). From available tables, cephalic outlines corresponding respectively to infants weighing between 2,500 and 3,000 Gm., 3,000 and 3,500 Gm. and 3,500 and 4,000 Gm. were constructed. Due allowances were made for the normally flexed position of the fetal head during the process of birth. The inclusion of all three sizes on a



ities of any physician willing to spend the few hours necessary to learn the basic principles and techniques. After a minimal amount of practice, any pelvic diameter may be measured within limits of error of a few millimeters. Moreover, only two films, an anteroposterior and a lateral, and the very simplest of calculations are involved.

It is no part of the purpose of this paper to discuss roentgenologic pelvimetry, except to emphasize that it is necessary for determination of two of the essential measurements. It is doubtful if graphic portrayal of relative pelvic size is necessary in patients with average, or larger, manual measurements, since associated midplane contraction is unlikely. On the other hand, as manual measurements approach the lower limits of normal according to Litzmann and Williams, midpelvic contraction becomes increasingly probable, and the need for accurate study of the *entire* bony pelvis increases. When roentgenographic evaluation is necessary, it is obviously desirable to make all measurements from the films rather than to depend in part upon manual methods.

Standards of inlet and outlet contraction sufficient to modify the course of labor are well recognized and do not need to be repeated here. Standards of midplane contraction are not well established, but are rapidly being formulated as experience accumulates. This is quite understandable when we remember that outlet contraction was defined by Williams so recently as 1909, and that midplane contraction could be recognized readily only after the advent of roentgenographic mensuration. Midplane contraction has not received sufficient attention, although it is becoming increasingly apparent that it is a definite entity.

Ideally, it would be desirable to determine the six basic pelvic diameters necessary for graphic representation on all obstetric patients. It is becoming the practice at Parkland Hospital to measure them in all primigravidas, and each multigravida with a history of difficult labor. With ever-present financial restrictions, this is not always possible, and it is, therefore, desirable to establish indications for roentgenographic mensuration of the midpelvis. This will be the subject of a forthcoming paper.

### Summary

A method of graphic portrayal of size and approximate shape of inlet, mid-, and outlet planes is presented. This is accomplished by diagramming each plane on a graphic outline of its normal counterpart. Six measurements, the anteroposterior and transverse of the inlet and midplane, and their point of intersection, and the posterior sagittal and transverse of the outlet are sufficient for graphic portrayal. Four of the six measurements can be obtained, or closely estimated, manually. Roentgenographic mensuration is necessary for the transverse diameter of the inlet, the anteroposterior of the midplane, and the determination of the point of intersection of the two basic diameters of each of these levels. It is desirable for determination of the transverse diameter of the midplane. When roentgenographic mensuration is performed, it is obviously better to make all measurements from the films than to depend in part upon manual mensuration.

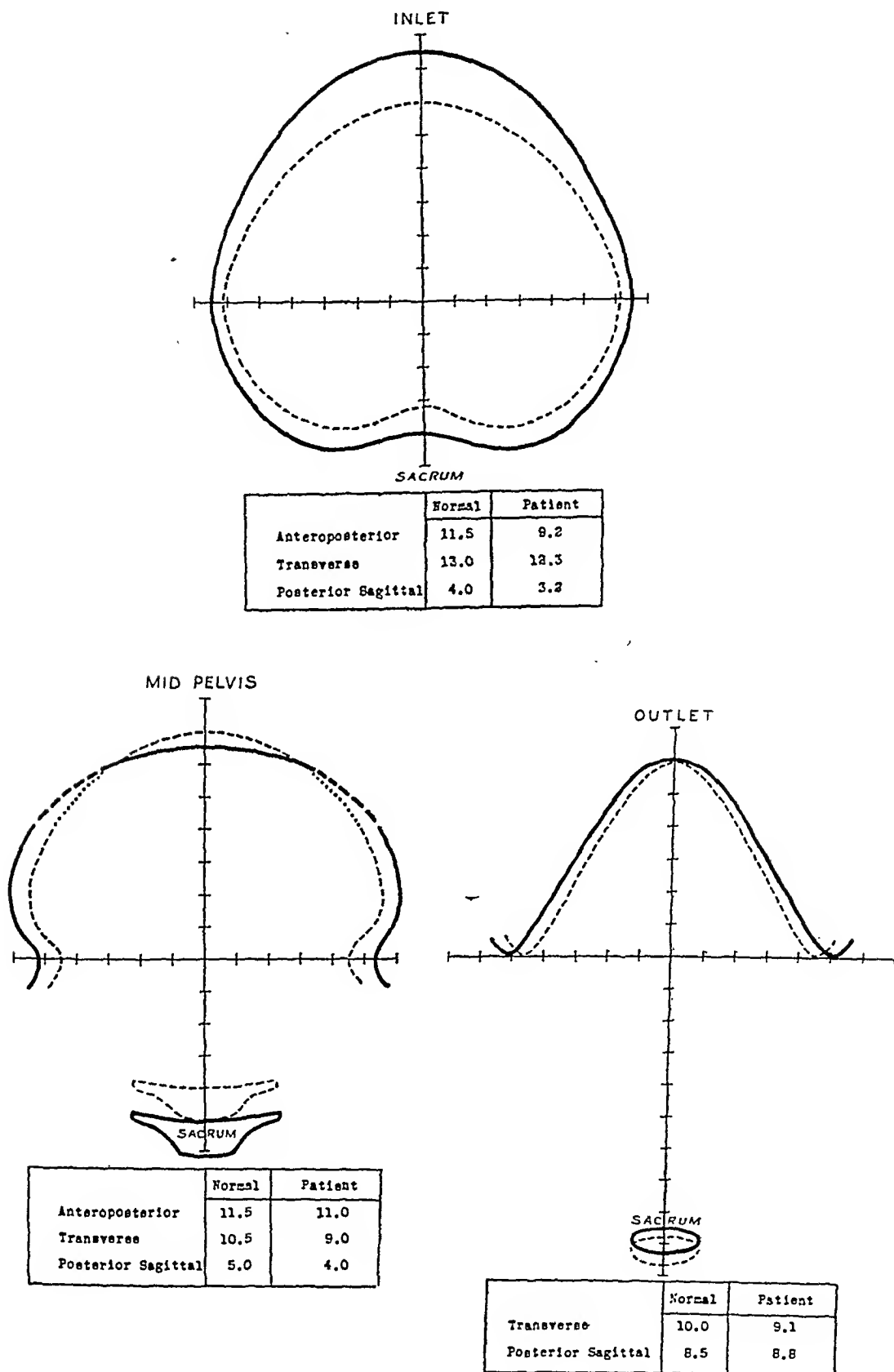


Fig. 4.—The dotted lines represent graphically the pelvis of patient E. M. It was predicted that engagement would occur in the transverse diameter of the inlet, that arrest would occur just above the midplane, and that the head would have to be drawn obliquely through the midplane with forceps. Furthermore, completion of rotation to a direct occipitoanterior below this level would be followed by easy extraction. This is precisely what happened. The second stage of labor lasted three hours and forty-five minutes.

(Slide.) This is a person who had some inlet contraction, slight midplane contraction, neither very well marked but very definite, and the outlet was normal. We felt that it was quite possible for her to go ahead with her labor and so we allowed that to continue. The head has already a certain degree of moulding, but even before that phase we thought it would be all right.

The lateral view shows the posterior sagittal about 1 cm. shorter than the average normal. In this case the head became arrested at the level of the spines, necessitating a very difficult midforceps operation. Fortunately, the baby was all right and the mother suffered only a moderate degree of soft parts injury. Of course, if one gets accurate measurements, we can recognize a marked degree of contraction, and those patients should be delivered by abdominal operation rather than by dragging the baby through with midforceps.

One of the things that radiographic methods particularly bring out is the shape of the pelvis. The old manual techniques gave us some idea about measurements, but told us nothing of the shape of the pelvis.

This picture is rather startling at first, and if one had only that to go on one would say that this woman could not possibly have a spontaneous delivery. Yet she did have a normal spontaneous birth.

(Slide.) This is another rather startling one discovered on x-ray, an old fracture. They are increasingly common in these days of automobile accidents. The question was: could this patient have a spontaneous delivery, and should we let her go into labor? She had a quick, two-hour labor.

I believe that this radiographic method presented should prove of considerable value. Dr. Mengert's opinion evidently differs somewhat from that of Dr. Thoms in that we can have a normal outlet and normal inlet more often than we realize, and yet have isolated midplane contraction.

DR. GEORGE KAMPERMAN, Detroit, Mich.—I am a little dubious about the interpretation of this method of pelvic study. Dr. Mengert rather deprecates radiologic measurements because of the distortion of structures. Yet, the two most important measurements he uses are obtained by radiologic methods. I would judge that this might at once throw an error into the study. Judging from his enthusiasm, I expect he has found some way of overcoming the possible error. One could be somewhat dubious, however, when the two most important measurements are somewhat uncertain.

DR. MENGERT (Closing).—I was taught that contraction of a degree to cause dystocia occurred most often at the inlet, seldom at the outlet, and almost never at the midpelvis. Since then it has become obvious that midpelvic contraction occurs more often than outlet, and probably more often than inlet contraction.

The bony pelvis is not very tall, since its total height is 5 cm. anteriorly and 10 cm. posteriorly. If one knows the contour of three cross sectional planes, he will have all necessary information regarding the bony pelvis. If the top and bottom cross-sections are of sufficient size, average or better, there is little chance of serious midplane dystocia. On the other hand, if the top and bottom cross-sections are at the lower limit of normal, there is good chance of midplane contraction; a sort of hourglass type of pelvis. My interest in this began many years ago with just this type of patient with inlet and outlet measurements within the normal range, but at the lower limit of normality. She had a midplane contraction necessitating a difficult midforceps extraction, with a resulting dead baby.

Since each of the three essential planes can be depicted graphically from knowledge of two diameters, it is necessary to ascertain these measurements. Three of them can be obtained very well manually. The other three are not so readily measured, and one of them, the transverse of the inlet, is impossible to measure manually. Therefore, in actual practice we depend on the x-ray for measurement of the transverse of the inlet and for the transverse and anteroposterior diameters of the midplane.

Any of the various and current x-ray techniques will give satisfactory measurements within a few millimeters.

By means of graphic portrayal of relative pelvic size, accurate prognosis is possible. It is also possible to make precise prognosis of modifications of the course of labor occasioned by mild cephalopelvic disproportion.

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### Discussion

DR. HENRY C. HESSELTINE, Chicago, Ill.—Drs. Mengert and Eller are entitled to forthright commendation on this presentation, for their contribution offers an ingenious method for evaluation and visualization of pelvic planes. The apparent ease and precision of mensuration invite further study. By using the same methods and units of measure, scientific comparisons are possible. As Dr. Mengert indicated, the one purpose of this paper was to present a method for depiction of the pelvic planes, especially the midplane.

We at the Chicago Lying-in Hospital have not had an opportunity to try this method yet. We employ routinely the basic measurements of the conjugate diagonals and bisischial diameters and general palpation for pelvic alteration. This last reference includes degree of prominence of ischial spines, changes in the sacrum and other parts of the bony pelvis. Whenever measurements under the normal limitation or variations are encountered, special and individual attention is given to the patient. At this time, we may use the Caldwell and Moley classification, as an additional prognostic aid.

Internal pelvic measurements give us only the maximum space available. These concrete measurements do not offer any information about the soft tissues of the pelvis. These efforts to determine pelvic size in no way shed light upon the quality of labor which may be expected. Although the essential pelvic diameters may be accurately determined, it is not possible to be as exact on fetal size and mensuration.

We teach that the sequence of labor and delivery by the vaginal route takes place not by the rule of simple formula, but because there are multiple favorable factors. These factors as we all know them are: the available and usable pelvic capacity, the physiologic elastic pelvic soft tissues, good quality and quantity of uterine contractions with normal uterine mechanisms, and, finally, a passenger that can conform to these conditions without alteration or by physiologic molding.

As we become more adept in discovering or predicting the deviations from normal, the more we may safeguard the welfare of the mother and her baby. For this reason alone, this contribution of Mengert and Eller is valuable.

I urge Dr. Mengert to continue with his proposed program, to give it a clinical trial, and to explore the various uses and limitations. Until then, caution must be presented lest those inexperienced with these tools and unacquainted with their use employ this procedure incorrectly or, possibly, dangerously.

Thoms and Schumacher (*AM. J. OBST. & GYNEC.* 48: 52, 1944) in their article "The Clinical Significance of the Midplane Pelvic Contraction," said, . . . "We wish to emphasize that although the knowledge of essentially exact pelvic measurements should never replace sound clinical judgment, which obviously includes the evaluation of the size of the child, character of the labor, etc., the intelligent consideration of such knowledge should form an important aspect of scientific obstetrics."

DR. KARL M. WILSON, Rochester, N. Y.—This method that Dr. Mengert presents impresses me as one of value and a very ingenious one which should be extraordinarily helpful. However, radiographic methods, after all, really offer the only satisfactory—in fact, the only possible means of obtaining accurate measurements of the midplane, corresponding rather closely to what used to be called the plane of least pelvic dimensions. The importance of this region as a site of dystocia is considerable, of course, and all of us, I am sure, have had the experience of arrest of the head in this region and a delivery completed by a difficult midforceps operation. What we want, of course, is an accurate method of radiographic cephalometry, but of that we have no hope.

amytal by mouth, one hour before operation. In all cases the abdomen is prepared and draped for operation and a local anesthetic of 0.5 per cent procaine hydrochloride may be used. At present we are using continuous caudal analgesia in selected cases and occasionally continuous spinal anesthesia if labor is progressing unusually rapidly. We have found these methods to be especially applicable to early postpartum sterilization. Immediately after delivery the

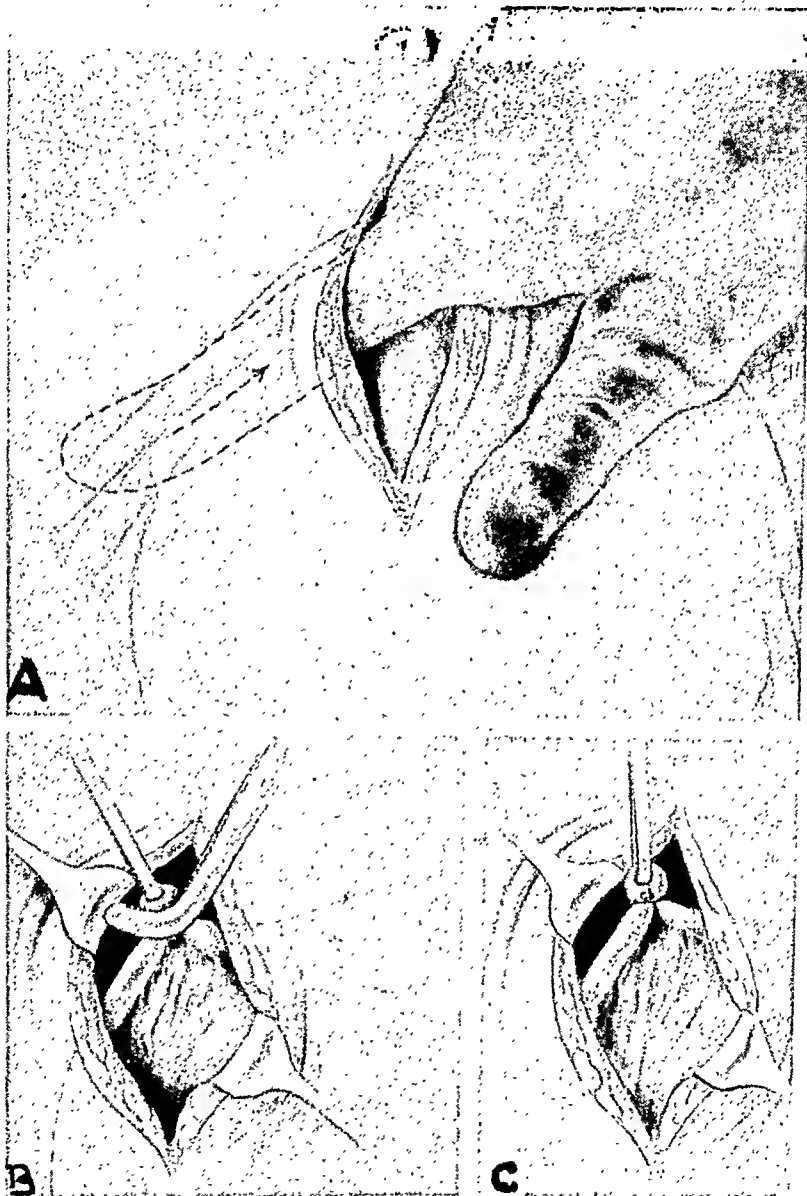


Fig. 1.—A. The index finger is inserted into the abdominal cavity and over the round ligament through a subumbilical incision one and one-half inches long. The uterus is rotated to bring the fallopian tube into the incision.

B. The fallopian tube is elevated with an Allis forceps and crushed with a heavy clamp.

C. The clamp is replaced by a ligature of heavy silk.

uterus is an abdominal organ rather than pelvic and, therefore, more easily approachable than after involution has taken place. The fundus of the newly delivered and contracted uterus is readily palpable, and at this level in the midline below the umbilicus, an incision one and one-half inches in length is made through the skin, subcutaneous fat, fascia, and peritoneum. This affords sufficient space to insert the index finger over the round ligament (Fig. 1-A). The

# THE TIME FOR POSTPARTUM STERILIZATION\*

## Report of 150 Cases Bacteriologic Studies on the Postpartum Uterus

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WITH THE ASSISTANCE OF

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IN 1936, I suggested early postpartum sterilization. Adair and Brown,<sup>1</sup> in 1939, kindly acknowledged the suggestion, extended the time for operation to within the first twenty-four hours after delivery and reported 50 cases. They were well satisfied with their results. In 1940, Hewitt and Whitley,<sup>2</sup> using the same technique, reported a study of 100 patients sterilized by this method one hour following delivery and were also enthusiastic in support of the procedure. Although we have frequently employed the Pomeroy technique and found it to be satisfactory, only the Madlener type of tubal sterilization is included in this report. It is not intended that the relative merits of the Madlener, Pomeroy, and other methods of sterilization be discussed, but rather the time for postpartum sterilization.

That occasions arise in obstetric practice when prevention of pregnancies is imperative to the future welfare of a mother and her family is commonly accepted. Such situations are usually associated with those toxemias of pregnancy, the damage from which is augmented by future pregnancies, as well as with tuberculosis, cardiac, renal and mental diseases, and other conditions. Multiparity may be the predominant issue, or a combination of circumstances may combine to form an indication for sterilization.

### History

In 1919, and twice thereafter, Madlener<sup>3-5</sup> described the method of sterilization which bears his name. The technique is almost entirely based upon the work of Friedemann<sup>6</sup> who, in 1906, reported one case in which he crushed an area in both Fallopian tubes by means of the Mikulicz clamp, but recommended the Doyen clamp (later used by Madlener) and ligated the crushed area with catgut. He did not mention ligating a knuckle of the tube, nor did he use nonabsorbable suture material for the ligature, but otherwise the method was the same as that described by Madlener. There have been several modifications of this technique and some controversy as to its reliability, but the method as detailed by Madlener has given encouraging results.

### Method

If an analgesic has been used during labor, many patients are still feeling the effects soon after delivery. However, to insure the patients' comfort 0.01 Gm. of morphine sulfate may be given by hypodermic injection or 0.2 Gm. of sodium

\*Read (by invitation) at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

social and economic conditions. All of Group 1 had given birth to five or more babies—some to as many as twelve, and the average parity was 5.6, while in Group 2 the average parity was 6.7, and some had given birth to as many as fifteen babies. We considered that such a woman had done her duty, and that the children in the family were entitled to the future protection of the mother. Anemia, unless severe, was not included as an indication, for a considerable proportion of all our indigent patients are anemic as judged by the usual standards.

TABLE II. GENERAL INFORMATION

	GROUP 1	GROUP 2
<i>Age and Parity</i>		
Average parity	5.6	6.7
Average age	33 yrs.	28.2 yrs.
<i>Mortality, Morbidity, and Stay in Hospital</i>		
Mortality	0	0
Morbidity	12.5%	6%
Average stay in hospital	13 days	9 days
<i>Length of Labor</i>		
Shortest labor		1 hr.
Longest labor		46 hrs.
Average labor	10 hrs.	12 hrs.
<i>Time Elapsing Between Delivery and Operation</i>		
Shortest interval	1½ hrs.	1 hr.
Longest interval	8 hrs.	18 hrs.
Average interval	2½ hrs.	3½ hrs.
<i>Type of Delivery</i>		
Breech assisted	1	5
Low forceps	2	3
Spontaneous	47	92
	50	100

Forty-seven patients in Group 1 delivered spontaneously, two were delivered by low forceps, and one by breech extraction. In Group 2, 92 were spontaneous deliveries, and eight were assisted. The average age in Group 1 was thirty-three years, and average duration of labor ten hours; while in Group 2 the average age was twenty-eight years, and the average length of labor was twelve hours. The average stay in the hospital was thirteen days in Group 1 as compared with an average postpartum hospitalization of nine days for patients in Group 2. This compares closely with the average obstetric hospitalization without intervention of this nature. These operations in each series were done by approximately twelve members of our house staff under the supervision of the resident physician. There was no mortality, thrombosis, or embolism in either group, and, according to the standard approved by the American Committee on Maternal Welfare, the morbidity was 12.5 per cent for Group 1 and 6 per cent for Group 2. The standard mentioned is that any patient with a temperature of 38° C. (100.4° F.) or more on any two days after the first twenty-four hours postpartum, oral temperature readings being made at least four times daily, is febrile. There was one postoperative complication in each series, and that was wound infection which prolonged hospitalization to about three weeks.

#### Time for Operation

The time when this operation should be done in the postpartum period is the crux of the situation, and the technique used in this report is that of Madlener. By early postpartum sterilization, it is not meant to disturb the patient by surgical intervention the instant her baby is born, but rather to carry out the procedure as soon after delivery in well selected cases as is consistent with good

uterus is moved or rotated on its longitudinal axis to bring the corresponding Fallopian tube into the incision, where it is seized with an Allis or Babcock clamp and lifted upward. The knuckled tube, including a small portion of the mesosalpinx, is clamped across with a crushing instrument. This must be carefully done to paper thinness and without breaking the serosa, as recommended by Madlener.<sup>3</sup> At first we used a crushing intestinal clamp for this purpose, but, finding it inconvenient to use in a small area, substituted a heavy clamp with a short powerful jaw 9 mm. wide, provided with longitudinal serrations (Fig. 1-B). The Fallopian tube is thus doubly crushed, leaving the clamp in place for one-half minute, and ligated with double heavy black silk (Fig. 1-C). The procedure is repeated on the opposite tube, and the small abdominal incision closed in layers. It is more important to proceed carefully, especially in crushing and ligating the tube, than it is to hurry, but the operation should not take longer than fifteen to twenty minutes. Some authors have suggested placing a third ligature on the tube. This seems unnecessary and could be harmful. The crushed and ligated area which is proximal to the uterus is the important one, and, if the serosa is injured, resulting in a tuboperitoneal fistula at this point, a failure results regardless of other ligatures.

### Material

We present a résumé of 50 postpartum sterilizations performed in the Department of Obstetrics and Gynecology of the Peiping Union Medical College during the years 1939 and 1940, by the technique just described and a series of 100 cases from the Department of Obstetrics and Gynecology of the University of Tennessee College of Medicine from 1939 to 1946. There is nothing in common between the Chinese and American series other than that the time and technique of operation are the same, and the indications are similar. We do not intend to go into the details of individual cases. The indications in general for both groups were as shown in Table I. Henceforth in this discussion the series of cases from Peking will be mentioned as Group 1, and the series from Memphis as Group 2.

We did not operate upon any patient with actual or potential infection as far as we could judge. Multiparity was included as an indication for sterilization, inasmuch as most of these were indigent patients who live under poor

TABLE I. INDICATIONS FOR POSTPARTUM STERILIZATION

	GROUP 1	GROUP 2
Multiparity	23	33
Multiparity with pre-eclampsia	5	5
Multiparity with eclampsia	0	2
Multiparity with anemia	3	9
Hypertensive cardiovascular disease	2	12
Essential hypertension	0	4
Varicosities	0	4
Pulmonary tuberculosis	6	4
Renal disease	0	16
Hydronephrosis	0	1
Nephrosclerosis	0	1
Lymphopathia venereum	0	1
Hyperthyroidism	0	1
Myocardial insufficiency	0	1
Rheumatic heart disease	10	0
Bronchial asthma	0	2
Polycythemia vera	0	1
Diabetes mellitus	1	1
Mental deficiency	0	1
Psychosis	0	1
	50	100



## CONTINUOUS SPINAL ANALGESIA IN CESAREAN SECTION\*

### Its Advantages, Technique, and an Analysis of Three Hundred Cases

JOHN C. ULLERY, M.D., F.A.C.S., PHILADELPHIA, PA.

THE administration of regional or local analgesics for operative procedures has gained increasing prominence in the past few years and, with improvements in technique and drugs, their use should supplant, in a large measure, the older types of general anesthetic agents now employed.

Cesarean section<sup>1</sup> requires a more careful selection of anesthesia than any other surgical obstetric procedure. Here, consideration must be given to the child in utero as well as to the mother, and an anesthetic must be used that will be satisfactory to both. The ill effects of various drugs and inhalation anesthesia on the unborn child have long been recognized. The marked narcosis of babies delivered by these methods has been one of the highest causes of fetal mortality. Realizing this deleterious effect, it has become the object of obstetricians, when cesarean section is indicated, to use an anesthetic agent which will have the least possible effect upon the baby.

With the advent of spinal anesthesia, it was thought that a method had been found that would be safe for the baby, but at that time only drugs of high toxicity were available and large doses were injected. As a consequence, numerous deaths occurred before the operation began. As a result of this maternal mortality, single dose spinal anesthesia was given up in most of the clinics throughout the country and local infiltration was used as safest for the mother and child. However, not every patient was suitable for this type of anesthesia and inhalation agents were used in a high percentage of cases. Since the introduction of continuous or fractional spinal by Lemmon,<sup>2</sup> in 1939, and with the use of less toxic drugs, its safety has been well demonstrated. The application of this method to cesarean operations followed, in that it offered an ideal method of safety and controllability which is so necessary for the operation.

*Definition.*—Analgesia is defined as the production of an insensibility to pain and is used here instead of the common term anesthesia, which usually denotes complete absence of sensation. Thus continuous spinal analgesia means only a loss of sensibility to pain and the complete retention of consciousness, produced by the injection of a drug into the subarachnoid space.

#### A. Advantages.—

1. The safety of continuous spinal analgesia lies mainly in the administration of smaller initial doses instead of the previous one-injection method. This is because the most dangerous period of spinal analgesia is within the first thirty minutes after injection. With the giving of a small initial dosage of the drug any untoward toxic symptoms will be minimal, and with the needle in the subarachnoid space, most of the drug can be rapidly withdrawn by removing several cubic centimeters of cerebrospinal fluid.

2. The controllability of continuous spinal analgesia is of paramount importance in cesarean section. A very small dose of the drug is given to reach

\*Read at a meeting of the Philadelphia Obstetrical Society, Nov. 1, 1945.

judgment, and with due regard to the local and general condition of the patient. Following infection as manifest by the presence of fever, the most frequent and serious complication of the immediate postpartum period is hemorrhage. In recognition of this fact, the rules of hospitals require, or should require, that the patient remain in the delivery room undisturbed for one hour after delivery, or until the period of bleeding is over. In the absence of bleeding at the end of one to two hours after delivery, one may assume that there is little danger of hemorrhage. Skajaa<sup>7</sup> sterilized 126 patients by the Madlener technique from the second to the twenty-ninth days postpartum. There were seven cases of thrombosis and one of embolism in the group operated upon after the fourth day. The uterus and other pelvic organs were disturbed at the height of involution and at a time when the uterus contains pathogenic bacteria, as has been shown by studies on the bacteriologic condition of the puerperal uterus. Skajaa also reported one case of thrombosis occurring in a patient sterilized on the second day. In a study of the bacteriologic condition of the puerperal uterus, by means of intrauterine cultures taken on an average of 3.2 days after delivery, Douglas and Rhees<sup>8</sup> found anaerobic and aerobic streptococci in 73.6 per cent of all patients studied. Loeser<sup>9</sup> found bacteria in the upper cervix in 25 per cent of his cases on the first day post partum. Kulka<sup>10</sup> believes that bacteria invade the uterus even during labor. Adair<sup>1</sup> and again Diamond<sup>11</sup> came to the sound conclusion that postpartum sterilization should not be done after the first twenty-four hours. Thornton and Williams<sup>12</sup> reported a group of 309 sterilizations, 178 of which were combined with appendectomy. There was a morbidity of 21 per cent, one fatality, thromboses, and other complications in those operated upon after the first day, and the highest morbidity was in those done on the eighth day. Still they conclude that there is no relation between the time of operation and the postoperative complications. It is not our policy to combine postpartum sterilization with any other elective procedure. Knight<sup>13</sup> has reported a series of postpartum sterilizations with a morbidity of 19.7 per cent. The only patients reported as having fever were those who were operated upon from the third to the sixth days postpartum. Still the author concludes that the fourth or fifth postpartum day is the safest time for performing this operation. It is probable that bacteria find their way into the uterus much sooner after delivery than is commonly appreciated. It is our opinion that postpartum sterilization can be done by this method with a considerable degree of safety in well selected cases within the first few hours after delivery, but in view of the dangers of hemorrhage and infection, the patient is best protected by carrying out the procedure from one to two hours after delivery. The average time elapsing between delivery and sterilization was one and one-half hours for Group 1 and three hours for Group 2. Not included in this report were three cases who were operated upon on the third, fourth, and sixth postoperative days, contrary to the policy of the department. Two of these cases were morbid.

### Reliability of the Madlener Operation

Failures have been reported in regard to this type of operation on the tubes as in most operations for sterilization. Rubovits and Kobak<sup>14</sup> found endosalpingiosis in one case, and Adair<sup>15</sup> found tuboperitoneal fistula in two cases as causes of failure. Dippel<sup>16</sup> has reported five failures, four of which were due to avoidable causes, whereas the fifth, due to endosalpingiosis, was probably unavoidable. On the other hand, this type of tubal operation has had considerable success. In 1932, Madlener<sup>3</sup> reported that 86 patients previously reported had had no pregnancies in a period of nine years, and a review of reports in the literature totaling 4,279 patients sterilized by Madlener's technique, v. Graff<sup>17</sup> found that the operation was successful in 99.6 per cent of the cases. We have been handicapped in an attempt to follow these patients because the war made

it impossible to follow up Group 1, and there has been insufficient time to follow Group 2, but we know that one patient from Group 1 and two from Group 2 became pregnant after sterilization.

### Advantages

The advantages of early postpartum sterilization are evident. It is simple, safe, and relatively bloodless. Methods of contraception are often unreliable. Patients in whom sterilization is imperative and who are instructed to return to their physician months after delivery for this purpose, seldom do so unless pregnant. An operation to sterilize even ten to fifteen days after delivery must be considerably more extensive, thereby increasing the risk. The necessity of doing a cesarean section for the purpose of sterilization, although probably frequently done, is hereby eliminated. Future hospitalization for this purpose is avoided, and the postpartum hospitalization prolonged but slightly, if at all. It, therefore, has important economic aspects. The disadvantages of the development of infection or failure to sterilize are mostly, but not entirely, due to poor selection of cases and mistakes in technique.

### Studies on the Bacteriology of the Postpartum Uterus

Some of the classical contributions to the study of the bacteriology of the puerperium, such as those of Schottmüller,<sup>18</sup> Schwarz and Dieckmann,<sup>19</sup> Colebrook and Hare<sup>20</sup> and others, have been done in relation to puerperal sepsis. In forming a judgment as to the proper time to carry out this procedure or any manipulation of the puerperal uterus, it is necessary to consider the bacteriology of the normal, newly delivered uterus. Only in this way can infections such as phlebitis and thrombosis be avoided. With that in mind, we attempted a study to determine the time of bacterial invasion of the uterus after delivery. Uterine cultures were taken on 100 patients who had delivered through the natural passages, and none of the patients was operated upon. There was no selection of patients except that only nonfebrile patients were included in this series. Only three patients had a temperature as high as 99.4° F. and on only one occasion. Only one culture was taken on each patient, and no patient had fever after taking the culture. Uterine cultures were taken on patients in groups of 10 at the end of two, four, six, eight, and ten hours, and at the end of the first, second, third, fourth, and fifth days.

### The Technique of Taking Cultures

With the patient lying on her back, the perineum was cleansed with sterile water. With the legs flexed, the labia were separated and a bivalve speculum inserted to expose the cervix. A modified Little<sup>21</sup> tube was inserted through the cervix into the uterine cavity without touching anything on the way. The Little tube had been sterilized while wrapped in heavy paper. The tube was unwrapped, the culture taken, the tube rewrapped and placed in a sterile, covered, porcelain container, and taken to the laboratory. Immediately upon receipt in the laboratory, the Little tube was removed from its sterile paper wrapping, flamed, and the contents allowed to run into a tube of sterile saline. Aerobic and anaerobic cultures were completed on all specimens. The resultant suspension was then planted for study as follows:

*Aerobic Culture.*—A tube of veal and brain infusion broth, a blood agar plate (human blood being used), and an eosin-methylene blue agar plate were incubated at 37° C. and examined at the end of twenty-four and forty-eight hours. If negative, the plates were discarded and the broth examined again five days after taking the culture before the specimen was declared negative. If, at this time, the broth was positive, plates were streaked from the broth.

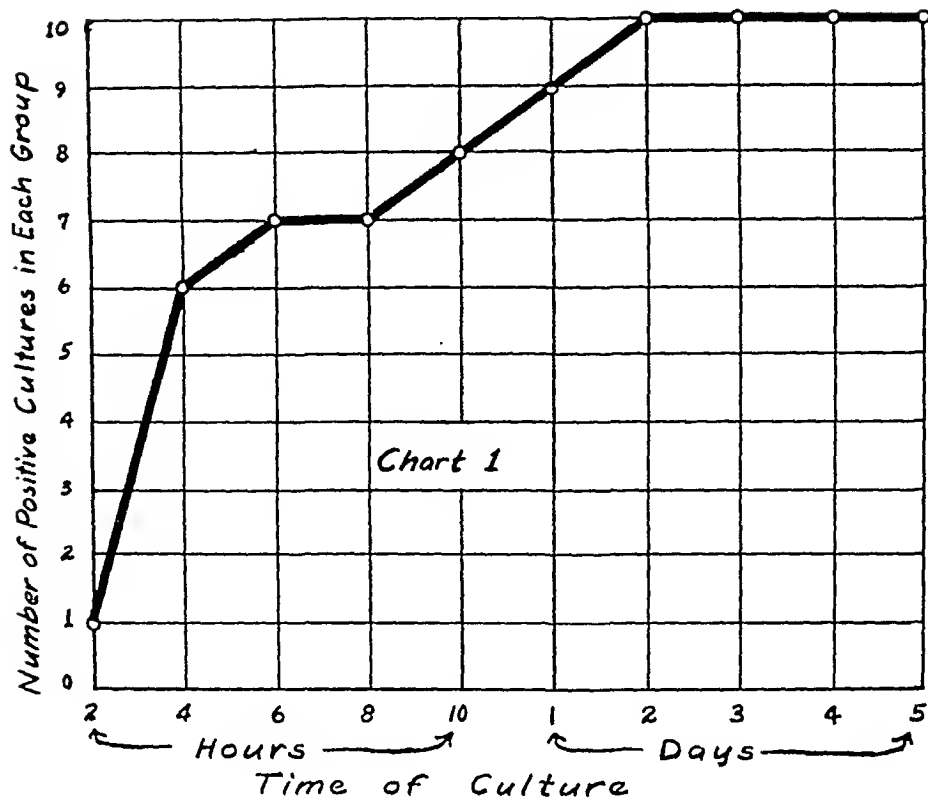


Chart 1.

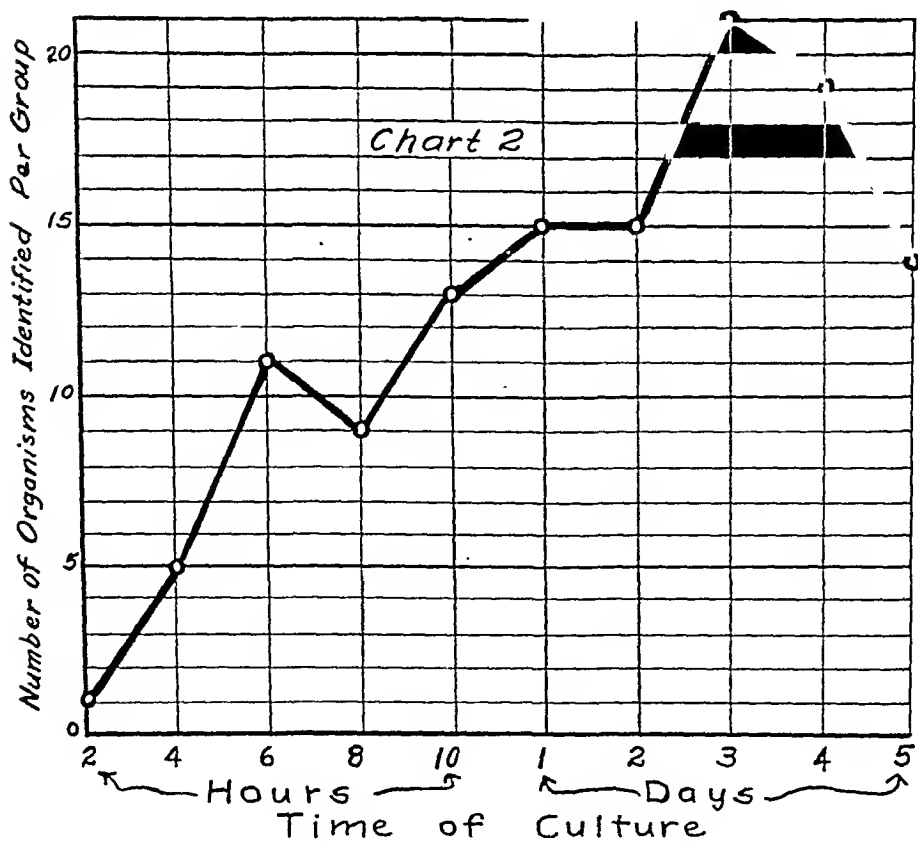


Chart 2.

**Anaerobic Culture.**—A tube of broth and a blood plate were incubated for forty-eight hours under anaerobic conditions, using the phosphorus method, and then examined. If negative, the broth was re-examined when five days old before being discarded.

**Carbon Dioxide Culture.**—Chocolate agar plates were liberally streaked and examined after forty-eight hours under carbon dioxide tension. The method of Wadsworth was used.

TABLE III. PERCENTAGE OF OCCURRENCE OF ORGANISMS IN POSITIVE CULTURES  
123 ORGANISMS FOUND IN 87 CASES

Anaerobic <i>Streptococci</i>		39 per cent
hemolytic	20 per cent	
nonhemolytic	19 per cent	
Aerobic <i>Staphylococci</i>		17 per cent
hemolytic	3 per cent	
nonhemolytic	14 per cent	
Aerobic <i>Streptococci</i>		15 per cent
hemolytic	6 per cent	
nonhemolytic	9 per cent	
<i>Escherichia coli</i>		14 per cent
Gram positive sporulating bacilli		8 per cent
<i>Bacterium aerogenes</i>		6 per cent
Diphtheroids		6 per cent
Anaerobic gram negative sporulating bacilli		5 per cent
Hemophilic bacilli		3 per cent
<i>Neisserian</i> group		3 per cent
Anaerobic hemolytic <i>Staphylococcus aureus</i>		2 per cent
<i>Bacterioides</i>		2 per cent
<i>Monilia</i>		1 per cent
<i>Actinomyces</i>		1 per cent
<i>Micrococcus tetragenus</i>		1 per cent

Saprophytic organisms were found in 19 per cent of the positive cases, but in only 5 per cent were they found alone. In all other instances they were found in association with one or more pathogens.

TABLE IV. ORGANISMS FOUND AND NUMBER OF TIMES ISOLATED PER GROUP

(Part 1)				
	Hemophilic bacillus, probably <i>H. influenzae</i>	Nonhemolytic <i>Staph. albus</i>	<i>B. aerogenes</i>	
	(1)	(1)	(3)	
	Nonhemolytic <i>Staph. aureus</i> , anaerobic	Gram neg. sporulating bacillus, anaerobic	Gram neg. sporulating bacillus, anaerobic	
	(2)	(1)	(2)	
<i>Actinomyces nocardia</i>	Beta hemolytic <i>Streptococcus</i>	Beta hemolytic <i>Streptococcus</i>	Nonhemolytic <i>Staph. aureus</i>	
(1)	(1)	(1)	(1)	
Nonhemolytic <i>Streptococcus</i>	Diphtheroid, unidentified	<i>Bacterioides</i> , unidentified	Nonhemolytic <i>Staph. albus</i>	
(1)	(1)	(2)	(2)	
Hemolytic <i>Staph. aureus</i>	<i>Monilia albicans</i>	Gram positive sporulating bacillus	Beta hemolytic <i>Streptococcus</i> , anaerobic	
(1)	(1)	(1)	(1)	
Nonhemolytic <i>Staph. aureus</i>	Nonhemolytic <i>Streptococcus</i> anaerobic	Beta hemolytic <i>Streptococcus</i> , anaerobic	Nonhemolytic <i>Streptococcus</i> ,	
(1)	(3)	(2)	(2)	
Beta hemolytic <i>Streptococcus</i> , anaerobic	Beta hemolytic <i>Streptococcus</i> anaerobic	Nonhemolytic <i>Streptococcus</i> , anaerobic	Gram positive sporulating bacillus	
(1)	(2)	(1)	(2)	
2 hours	4 hours	6 hours	8 hours	10 hours

TABLE IV—CONT'D—(Part 2)

			Hemolytic <i>Staph. albus</i> (1)	
			Diphtheroid, unidentified (1)	
			Nonhemolytic <i>Staph. aureus</i> (1)	
		<i>B. aerogenes</i> (1)	Beta hemolytic <i>Streptococcus</i> , anaerobic (2)	
Nonhemolytic <i>Staph. albus</i> (1)		Nonhemolytic <i>Staph. aureus</i> (2)	Nonhemolytic <i>Staph. albus</i> (1)	
<i>E. Coli</i> (2)		Nonhemolytic <i>Streptococcus</i> (3)	Nonhemolytic <i>Streptococcus</i> (1)	<i>E. Coli</i> (2)
Nonhemolytic <i>Streptococcus</i> (2)	<i>E. Coli</i> (3)	<i>B. xerosis</i> (1)	<i>E. Coli</i> (3)	<i>B. xerosis</i> (2)
Beta hemolytic <i>Streptococcus</i> (1)	Nonhemolytic <i>Streptococcus</i> (1)	<i>E. Coli</i> (4)	<i>B. subtilis</i> (1)	<i>B. aerogenes</i> (2)
Beta hemolytic <i>Streptococcus</i> , anaerobic (2)	Nonhemolytic <i>Streptococcus</i> , anaerobic (4)	Diphtheroid, unidentified (1)	Micrococcus tetragenus (1)	Hemolytic <i>Staph. aureus</i> (1)
Nonhemolytic <i>Streptococcus</i> , anaerobic (2)	Beta hemolytic <i>Streptococcus</i> , anaerobic (2)	Nonhemolytic <i>Staph. albus</i> (1)	Nonhemolytic <i>Streptococcus</i> anaerobic (3)	Alpha hemolytic <i>Streptococcus</i> (1)
Nonhemolytic <i>Staph. aureus</i> (2)	Nonhemolytic <i>Staph. aureus</i> (1)	Beta hemolytic <i>Streptococcus</i> , anaerobic (5)	A. hemolytic <i>Streptococcus</i> , anaerobic (1)	Beta hemolytic <i>Streptococcus</i> (1)
Gram positive sporulating bacillus (1)	Gram positive sporulating bacillus (2)	Nonhemolytic <i>Streptococcus</i> , anaerobic (1)	Member of <i>Neisseria</i> group (1)	Nonhemolytic <i>Streptococcus</i> (1)
Gram negative sporulating bacillus anaerobic (1)	Alpha hemolytic <i>Streptococcus</i> (1)	Member of <i>Neisseria</i> group (1)	Gram negative sporulating bacillus (1)	Nonhemolytic <i>Streptococcus</i> , anaerobic (3)
Hemophilic bacillus, probably <i>H. ducrey</i> (1)	Member of <i>Neisseria</i> group (1)	Gram positive sporulating bacillus (1)	Hemophilic bacillus, probably <i>H. influenzae</i> (1)	A. hemolytic <i>Streptococcus</i> , anaerobic (1)
1 day	2 days	3 days	4 days	5 days

A direct smear of each specimen was made after inoculation. Eight per cent of the cases showed bacteria on such examination, none of which was less than twenty-four hours post partum.

Special procedures used for identification of bacteria were as follows:

1. Bile solubility and capsule staining to differentiate *Streptococcus viridans* from the *Pneumococcus*. No *pneumococci* were found.

2. Oxidase dye test to confirm the presence of colonies of *Neisseriae*.

3. Coagulase test on *Staphylococci*. No *Staphylococci* were found with the ability to coagulate plasma.

4. Sugar fermentation reactions were used for the differentiation of diphtheroids, *Monilia*, and *Actinomyces*.

## Results

In 100 uterine cultures 87 were positive, 13 negative, and the latter occurred only among the cultures which were obtained during the first few hours.

Chart 1 gives eloquent evidence as to the time of bacterial invasion of the uterus after delivery. It will be noted that at the end of two hours, only 1 in 10 cultures was positive. At the end of four hours, 6 in 10 cultures were positive. At the end of six and again at eight hours, 7 in 10 cultures were positive. At the end of ten hours, 8 cultures were positive, while at the end of the first day, 9 of 10 were positive, and from the second to the fifth days all—that is, 40 consecutive cultures—were positive. It will be noted in Chart 2 that the number of organisms identified similarly increases up to the end of the third day and then the number decreases. It is possible that by the end of the third day, local and general immunities are beginning to become effective, but although the number of organisms had decreased, the cultures of the fourth and fifth days were markedly positive.

Table III illustrates that in the 100 uterine cultures taken, 123 organisms were found in the 87 positive cultures. Of the 123 organisms, 39 per cent were anaerobic *Streptococci*, 17 per cent aerobic *Staphylococci*, 15 per cent aerobic *Streptococci*, and 14 per cent *Escherichia coli*. It should be noted that although saprophytic organisms were found in 19 per cent of the positive cultures, they were found alone in only 5 per cent. Otherwise, they were always in association with one or more pathogens.

Table IV demonstrates the bacteria and the number of times which each was identified in each time group of these 100 uterine cultures. The least number was, of course, at two hours, and the greatest variety cultured was at the end of four days.

## Summary

The performance of early postpartum sterilization on nonfebrile patients has already stood the test of time. A group of early postpartum sterilizations from the Peiping Union Medical College, Peking, China, and the University of Tennessee College of Medicine, Memphis has been reported with studies on the bacteriology of the puerperal uterus. Studies on the normal postpartum uterus show that bacterial invasion occurs soon after delivery. It is clear that in many instances it might be necessary to wait a few hours after delivery before such a procedure is undertaken, but if the patient's condition is such that one should wait many hours, it is questionable as to whether it should be done at all, and certainly not after the first day. These bacteriologic studies also support the well-known clinical fact that the removal of membranes or fragments of placental tissue from the uterus shortly after delivery is relatively safe, whereas, the same procedure after the first postpartum day may be a dangerous intervention. With the patient in good condition, she is better protected by carrying out such a procedure in the early postpartum period. The optimum time to perform postpartum sterilization is from one to two hours after spontaneous delivery, which means that the period of probable postpartum hemorrhage is over, and the period of probable infection has not yet begun.

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### Discussion

DR. FRED L. ADAIR, Chesterton, Ind.—In discussing any operative procedure one should have three thoughts in mind: first, is it necessary; second, is it relatively safe in relation to the purpose to be accomplished; and, third, is it effective? It is generally agreed that there are certain conditions affecting women which make pregnancy a serious hazard to health and life, and where future pregnancies should be avoided.

The conditions would seem to be recognized in Dr. Whitecre's and also in the series of Dr. Brown and me. In a subsequent series collected by Dr. Dieckmann for another purpose, the indications remain practically the same, except that multiparity becomes somewhat more important. The indications regarding multiparity appear to be more economic and sociological than medical.

This operation affords one of the means of avoiding future pregnancies in those women where pregnancy constitutes a hazard to her life or health. The main hazard is from the possibility of infection. Originally, we attempted to distinguish between immediate, early, and late procedures. The first was done immediately following delivery, the second within the first twenty-four hours, and the last at some later period in the puerperium. It is well known, of course, that there is a bacterial ascending infection of the genital tract during labor itself, so it would seem that we should consider that factor in relation to infection. We should evaluate not only the actual labor itself, but the conduct of labor and the contraindications to the procedure. For reasons which seemed logical, we have carried out the early, or twenty-four hour, procedure. The bacteriologic studies presented indicate that from the point of the bacteriologic invasion of the genital tract this is the preferable time.

One of our contraindications was an abnormal labor. It should be kept in mind that the concentration of bacteria and the relation to the amount of lochial discharge may modify the number and variety of bacteria recovered by cultural methods. However, the main conclusion stands that the bacteria increase progressively in number and variety as the puerperium proceeds, and gradual involution leads to their decrease and elimination. While these organisms are obtained from the genital tract for technical reasons, it is very difficult to prove that they come from the uterine cavity itself.

The morbidity from this 24-hour procedure has been low and the mortality is nil. A point of importance is that failure in about 5 per cent of the cases is higher than in those patients who had tubal ligation when the uterus was not about to undergo involution. It may be due to the process of involution or also, possibly, to some imperfect technique. The operation is simple, but meticulous care is necessary to avoid subsequent fistulous formation or a restoration of the tubal lumen.

DR. EDWARD D. ALLEN, Chicago, Ill.—My discussion of this subject will have to be largely theoretical, because we have had no immediate experience with postpartum sterilization in my service. Sterilizations at the time of delivery have been limited to those indi-



cated following cesarean section or therapeutic abortion. Sterilization has not been used as a deciding indication for cesarean section, except in a very few borderline cases in whom previous obstetrical history has indicated that another pregnancy would probably occur before an operation during the early postpartum period could be done. If this or a similar type of patient can be safely delivered through the vagina, we believe they may be the only ones in which sterilization during the early puerperium is indicated.

We have not been able to prognosticate a normal puerperium accurately enough that we have felt justified in adding a laparotomy, however simple, to the risks already incurred by delivery. Some of our mortalities and many of the severe morbidities have occurred following uncomplicated delivery. In view of the results just reported by Dr. Whitacre, it would seem that in otherwise normal cases we are operating upon patients in whom a potential focus of infection will occur in twenty-four or forty-eight hours. It seems like crossing the railroad track when the red light is swinging; most often we will make it, but sometimes we will not. I do not know of anywhere else in surgery where we would choose these unfavorable possibilities.

Our departmental policy has been to delay sterilization until the pelvic organs have returned to normal except in those instances where the patient is already pregnant and therapeutic abortion followed by sterilization is indicated, especially in those patients in whom we have reason to believe that another pregnancy will occur if the sterilization is too long delayed. The morbidity and mortality in this pregnant group have been higher than in the nonpregnant series. The incidence of complications has increased with the duration of pregnancy. A more critical analysis of our results which is now being undertaken seems to indicate that in the future we will only undertake abortion and sterilization together for those unusual circumstances mentioned above. The results obtained in Dr. Whitacre's excellent study, I believe, will strengthen this decision.

We believe that sterilization by the vaginal route is safer than by the abdominal approach. In addition, if performed during the nonpuerperal state, it safely allows the additional procedures for cure of other pelvic complaints so commonly found in the patient needing sterilization. We have not included in these few statistics those cases of vaginal hysterectomy, of which there are a considerable number, done primarily for sterilization, but also to rid the patient of a bleeding painful uterus or partial prolapse. Eighty-nine of our sterilizations were done as a step in extensive plastic repair when hysterectomy was not indicated and the patient still in the childbearing age.

During the years from 1930 to 1944 there have been done on our service 210 vaginal sterilizations. One hundred and thirty-six of these were done on the involuted uterus and 74 following therapeutic abortion.

There has been one death which occurred forty-five days postoperatively from cerebral embolism in a patient who had been coincidentally aborted for endocarditis. Pregnancy occurred subsequently in three of these pregnant patients; all following cornual resection. As far as we can determine, no pregnancy has followed the other procedures, although no exact follow-up study has been made. In our hands, the smoothest results have been obtained by the modified Pomeroy. A loop in the midportion of the tube is crushed, tied with chromic catgut, and the looped portion of the tube removed. It is a simple, quickly done procedure, and statistically is as accurate as any procedure thus far reported in numbers large enough to be evaluated.

Eighty-three patients were sterilized by cornual resection, six had defundectomies, and in ten of the pregnant patients the products of conception were removed by hysterotomy and the tubal continuity interrupted by a modified Pomeroy. Twenty-five patients were aborted at 4 to 7 weeks term, 44 to 8 to 10 weeks, and 5 at 11 to 14 weeks. The average hospital stay of these patients was eight days. While those in the nonpregnant group required only 6.3 days. We are of the opinion that this length of stay in the hospital to undergo a relatively painless and safe operation is not sufficient indication to add even the minimal risk of abdominal sterilization to a newly delivered woman, unless her mentality or marital relationship will not permit of further delay.

DR. E. L. KING, New Orleans, La.—We have occasion at the New Orleans Charity Hospital to do this operation very frequently. Our chief indication is in the Negro multipara with cardiovascular disease. There are some other indications also, but the largest single group fall in that category. We have had 218 cases upon whom postpartum sterilization has been done in the past several years.

The time limit is somewhat different from that of Dr. Whitacre, but it has not seemed to interfere with the results obtained. We have not sterilized very many of these patients within the first few hours, the chief reason being not so much clinical or bacteriologic, but practical. We feel that it is necessary in these patients to obtain the written consent of both husband and wife. Many of these women of the renal-vascular group come in in labor or in a severely toxic state, and many of them are delivered within a few hours or a day after admission. Frequently it is a matter of several days before we can get the necessary papers signed. Besides that, to protect ourselves from criticism, we have to get the medical service of the Institution to agree that the patient should be sterilized, and that also takes time. So our sterilizations have taken place over several days to a week.

We have not had any mortality, but we realize, of course, that we are working with a uterus that has bacterial contamination. By tying an extra ligature around the tube on each side of the ligated loop, we think that we have improved the method. We can say that one patient has returned pregnant after this operation. The others have not been followed up.

DR. WHITACRE (Closing).—In regard to Dr. Allen's remarks, this procedure was intended in a special group of cases to avoid cesarean section which, it is clear, carries a low but definite mortality. Also, it avoids therapeutic abortion in some of these patients in the future.

It should be mentioned in relation to Dr. King's suggestion of extra ligatures in the tube, that the one most proximal to the uterus is the important one, for, if the serosa is broken, it might result in a tuboperitoneal fistula and, therefore, failure, regardless of other ligatures.

We have no intention of being dogmatic, but this study on the bacteriology of the puerperal uterus indicates this time when any manipulation of the puerperal uterus can be carried out with reasonable safety.

*(As it was not possible to include all of the papers presented at the meeting, the remainder will appear in the January number of the JOURNAL.)*

## Necrology

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DR. JOHN A McGLINN, associate professor of gynecology in the Post-graduate School of the University of Pennsylvania (retired), consultant to the Philadelphia General Hospital, the Fitzgerald Mercy Hospital, Phipps Institute, and St. Luke's Hospital, Vice-President of the American Gynecological Society in 1936, past President of the Philadelphia Medical and the Philadelphia Obstetrical Societies, Fellow of the American College of Surgeons, died on Nov. 29, 1946, in Philadelphia, at the age of 75 years.

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## Items

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### American Board of Obstetrics and Gynecology, Inc.

The next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 7, 1947.

Arrangements will be made so far as is possible for candidates to take the Part I examination (written paper and submission of case records) at places convenient for them. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held June 1 to 7, 1947, at Pittsburgh, Pa. Notice of the exact time and place of the Part I and Part II examinations will be sent all candidates well in advance of the examination date.

For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh, Pa.

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The following physician has completed all requirements for certification by this Board, and is included in the list of diplomates: Dr. Herschel Frank Connally, 1305 Amicable Bldg., Waco, Texas.

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### The International Congress of Obstetrics and Gynecology

The Congress will be held in Dublin, Ireland, during the week beginning July 7, 1947, to celebrate the Bicentenary of the Rotunda Hospital. Representatives from all parts of the world have signified their intention to participate in the presentation of an elaborate program which includes addresses and discussions on the history of midwifery, puerperal sepsis, eclampsia, sterility, puerperal mortality, and obstetric shock. Messrs. Thomas Cook and Son, Ltd., are the authorized travel agency and also accept registrations for the Congress. The Honorary Secretary is Mr. G. F. Klingner, Rotunda Hospital, Dublin.

the desired level just above the operative field. Usually this will suffice for the operation. Additional doses may be given if the operation requires longer. Thus, a very minimum of the drug can be used and at all times well controlled. If the level reaches too high or the blood pressure falls below a safe level, most of the drug can be withdrawn by aspiration.

3. The ease of administration is important. As the technique consists essentially in making and maintaining a spinal puncture, even the occasional operator can perform it easily. A spinal puncture is one of the easiest procedures in medicine, and with the addition of a few technical details the analgesia is easily given.

4. The speed of the procedure likewise offers certain advantages. Frequently a rapid cesarean section is imperative and, with the short time required for a spinal puncture plus administration of the drug, and its rapid action in producing analgesia, loss of blood to the mother and fetal mortality can be markedly lessened.

5. The decrease in postoperative complications following its use also makes it ideal. The reduction in post-operative nausea and vomiting with less abdominal distension than with inhalation agents is marked. Usually patients having continuous spinal analgesia for cesarean section can be fed the same day of operation, which eliminates many of the abdominal complaints. Urinary retention is no greater and phlebitis is probably less frequent, as also are pulmonary complications.

6. Excellent contraction of the uterine musculature, with minimal blood loss is outstanding. Few oxytocics are required following delivery of the baby.

7. The absence of narcosis to the baby offers one of the greatest advantages of this method. There is no need for resuscitation of the baby, as respiration is initiated usually before the baby is completely extracted from the uterus, and cries immediately. This is particularly valuable in premature infants born by cesarean section.

8. Excellent relaxation of the abdominal wall is an outstanding characteristic and enables the operator to perform his task with facility and dispatch. This is essential in Waters or extraperitoneal sections where relaxation is imperative.

9. Likewise, the anesthetic causes no disturbance of previously existing pathology in the respiratory, circulatory, or genitourinary system of the mother, as the drug is low in toxicity and the minimal dose is employed.

*B. Technique.*—The technique of administering the continuous spinal analgesia is as follows: The patient is given  $1\frac{1}{2}$  grains (0.1 Gm.) of a barbiturate one hour before operation, having been given sedation the previous night. When she is brought to the operating room she is placed upon a special mattress which prevents bending of the needle, and placed on her side. Under aseptic precautions the initial skin wheal of procaine is made between the first and second, or second and third lumbar interspaces, together with some form of vasopressor drug. Then the stainless steel safety needle is inserted into the subarachnoid space. With the needle in one of these interspaces, the drug will reach above the umbilicus and produce the desired level for the best results. Eight cubic centimeters of cerebrospinal fluid is withdrawn and mixed with the anesthetic drug, usually procaine hydrochloride, to make a  $2\frac{1}{2}$  per cent solution (25 mg. per c.c.), the syringe is then connected to the tube which is filled with the solution to expel the air. The tube is then connected to the needle and the initial dose is given. Each patient is treated as a special case, but the average dose is 25 to 40 mg. of procaine. She is then turned on her back, and placed in the 5° Trendelenburg position. The needle is then checked to determine whether it is still in the subarachnoid space. This is done by aspiration of the syringe. If no fluid is aspirated the needle must be adjusted until there is a

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free return flow. The length of time for analgesia to begin is usually five to ten minutes, during which time the abdominal field is prepared and draped.

The level of the drug is then determined by needle or forceps and, if satisfactory, the operation is begun. More drug, usually  $\frac{1}{2}$  c.c. ( $12\frac{1}{2}$  mg.), can be added if the level is not sufficiently high, but this is seldom necessary.

The blood pressure, pulse, and respiration are carefully taken every five minutes during the operation. The systolic pressure seldom drops more than 10 to 20 mm. of mercury, and many patients have less than 10 mm. fall. If the systolic level reaches 90 mm. or less,  $\frac{3}{4}$  grain of ephedrine HCl can be given hypodermically, or glucose-saline solution intravenously. Plasma should be available. In cases which show a profound fall in blood pressure a vasopressor drug can be given intravenously.

If the analgesia begins to wear off or the patient complains of any discomfort, additional doses of procaine can be given, usually in doses of  $\frac{1}{2}$  to 1 c.c. ( $12\frac{1}{2}$  mg. to 25 mg.).

After the baby is extracted  $\frac{1}{4}$  grain of morphine should be given hypodermically, which will reach its maximum effect after the anesthetic has been removed. Following delivery of the placenta, an oxytocic preparation (usually ergot) is given intramuscularly as a routine procedure. Following the completion of the operation the remaining drug is partially removed, by aspiration of 1 to 2 c.c. of fluid, and the needle withdrawn.

After removal from the operating room the patient is returned to her room, and placed flat in bed. Fluids and soft food can be given the same day.

*C. Indications and Contraindications.*—Continuous spinal analgesia may be used in all types of cesarean section. The condition of the patient, however, must be good. In the presence of severe hemorrhage from placenta previa or abruptio placenta where the general condition of the patient is poor it would be unwise to use continuous spinal analgesia. In cases of prolonged labor where cesarean section becomes necessary, supportive measures must be instituted before analgesia is given.

*D. Drugs.*—Either procaine hydrochloride or metycaine (1.5 per cent in Ringer's Solution) may be used as the anesthetic agent. Both possess low toxicologic drug reaction and give no depression of vital centers. They are easily obtainable and require small amounts. Their duration of analgesia is approximately the same, and neither cause any postoperative complications.

*E. Analysis of Three Hundred Cases of Cesarean Section Under Continuous Spinal Analgesia.*—In December, 1941,<sup>3</sup> we gave our first continuous spinal analgesia for cesarean section at the Philadelphia Lying-In Hospital. Since that time we have used it in three hundred cases there and at the Philadelphia General Hospital and Delaware County Hospital. At first our cases were carefully selected. But as time passed and its safety was well demonstrated, its administration has become almost routine for cesarean section, except as contraindicated above.

There were no maternal deaths. There were sixteen fetal deaths but none which could be attributed to the anesthesia. Their causes are listed as follows:

I. Stillborn	5
Abruptio placenta	4
Malpresentation	1
II. Neonatal	11
Prematurity	4
Cerebral hemorrhage	1
Congenital heart disease	2
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ably reduced over the inhalation anesthetics, as was postoperative distention. In a large majority of our patients fluids and food were given the same day of operation with good results. Indeed, it was the rule that the patients complained of hunger if not fed on the first day. Only two patients required exceptional treatment for distention, these being cases of prolonged labor before operation where Wangenstein drainage was necessary for relief.

In listing our indications for cesarean section, we have formed our own classification which follows closely that of other clinics. The apparent discrepancy in the number of indications in comparison to the total cases is due to the fact that some patients had more than one indication for the operation. For instance, several of our toxemias also revealed a cephalopelvic disproportion, or our previous sections were traced to disproportions which occurred in former deliveries.

TABLE I. INDICATIONS FOR CESAREAN SECTION

1. Cephalopelvic disproportion	102	
2. Pelvic tumors	16	
3. Premature separation of placenta	10	
4. Placenta previa	18	
5. Toxemia of pregnancy (including eclampsia)	20	
6. Cardiac disease	6	
7. Pulmonary disease	3	
8. Kidney disease	2	
9. Elderly primiparac	3	
10. Recent or extensive vaginal plastic surgery	18	
11. Elective cesarean section	a. Previous section	66
	b. Valuable baby	2
	c. Difficult previous delivery with questionable measurements	6
	d. Uterine anomalies	4
	e. Diabetes	3
	f. Prolapse of cord	3
	g. Malpresentation	22
	h. Rh syndrome	3
12. Dystocia syndrome	12	
13. Prolapsed colostomy with obstruction	1	

TABLE II

Endometritis	23
Pyelocystitis	12
Mastitis	9
Thrombophlebitis	2
Intercurrent infection	3
Dehydration	1
Morbidity—cause unknown	2
Wound infection	2
Atelectasis	1

Postoperative morbidity occurred in fifty-five patients (18.3 per cent). The standard classification of morbidity being used, i.e., an elevation of 102.2° F. or over on two successive occasions excluding the day of operation.

The type of cesarean section varied according to the indication and to the existence of any previous labor. In the patients with no previous labor the classical or Kerr type were performed. If labor had been present the Kerr or Waters section were procedures of choice.

TABLE III. TYPES OF CESAREAN SECTION

Classical	180
Kerr	104
Waters	12
Porro	4

The five stillborn babies were delivered of patients in whom cesarean section was performed for abruptio placenta in four cases, and in one where intra-uterine fetal death had occurred from malpresentation. No fetal heart sounds were elicited before operation, and in each case the baby's death was known. All the remaining babies born in this series, including prematures from 2 pounds, 14 ounces, cried at once, were quite vigorous, had good color, and showed no narcosis.<sup>4</sup> Thirty-six patients were or had been in labor for periods varying from six to sixty hours. In 264 patients cesarean sections were performed in which there had been no labor.

The ages of the mothers varied from 14 to 44 years, and the length of operation from fifteen to seventy minutes. The total dosage of procaine or metycaïne varied from 15 to 200 mg. In the beginning of the study 75 mg. was used as the initial dosage of the drug, but in the past six months this has been lowered to 25 to 30 mg., with satisfactory results. In many recent cases little, if any, more than the initial injection of 25 mg. has been required. Indeed, in one case in June, 1945, 15 mg. of metycaïne (1.5 per cent) was given as the initial dose and no more was required until the skin was being closed at the end of the operation. An additional 15 mg. maintained the analgesia until the patient was returned to her room.

The average systolic blood pressure in the three hundred patients before the administration of the analgesia was 127.5 mm. of mercury, and at the end of the operation was 120.5 mm. of mercury. Blood pressure readings were taken every five minutes. An initial dose of vasopressor drug, usually  $\frac{3}{8}$  grain of ephedrine hydrochloride, was given routinely, except in cases of hypertension where the systolic pressure exceeded 140 mm. of mercury. In twenty-nine patients the blood pressure fell to a systolic of 80 mm. of mercury, but returned to 100 or higher with the administration of ephedrine hypodermically or intravenously, or as soon as the baby was delivered. Frequently the elevation of the feet alone, that is, autotransfusion, would return the blood pressure to its normal level within two or three minutes, or the inhalation of 100 per cent oxygen would likewise aid in blood pressure elevation.

Nausea, retching, or vomiting were infrequent, and it was estimated that no more than 15 patients (5 per cent) showed this annoying complication. In each of these instances the inhalation of 100 per cent oxygen brought relief within one or two minutes.

Only five patients received venoclysis or plasma while on the operating table, three of these being patients who had long trials of labor and required fluids, one as a precautionary measure in the delivery of quadruplets, and one, who evidently showed a toxicity of the drug as her blood pressure fell from 122/82 before giving the spinal to 70/40 within two minutes after the initial injection of 75 mg. of procaine. After the infusion the pressure returned to normal.

There were nine failures in which the operation could not be performed under continuous spinal analgesia completely. Five of these were due to technical failure to introduce the needle into the subarachnoid space, and in four cases it was necessary to use a supplementary anesthetic, as the level was not sufficiently high to proceed with the operation. Sixteen doctors were included in the group who gave the spinal analgesia, some of whom had had previous experience with the single spinal injection anesthesia, and others, particularly the resident staff, who were giving spinal analgesia for the first time under our supervision.

Postoperative complications were no greater than with the inhalation anesthetics. Headache occurred in 5 per cent of the cases, urinary retention in 8 per cent. There were no motor or sensory disturbances. One pulmonary complication occurred; this was an atelectasis which required intermittent inhalation of oxygen plus postural treatment. Nausea and vomiting were consider-

## THE Rh FACTOR IN OBSTETRICS\*

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THE Rh factor in obstetrics has held the attention of the obstetrician and the laity for the past few years. Because of articles in lay women's magazines, many pregnant women have become Rh conscious, and have bombarded their obstetricians with numerous and varied questions regarding this rather important subject. As a matter of fact, many laboratory technicians and nurses have had this test performed on their own blood and, if negative, have by subterfuge or other means obtained a sample of blood from their prospective husband in order to determine his Rh factor. With the rare occurrence of erythroblastosis, this possible blood incompatability is not too serious and, as suggested by Diamond,<sup>1</sup> there are many far more serious incompatabilities in many husbands and wives than this Rh incompatability.

It is now generally accepted that Rh typing, in addition to the usual blood grouping and cross-matching, is essential in order to insure maximum safety in blood transfusions. This is especially true in cases where multiple transfusions have to be administered. According to Diamond,<sup>1</sup> 80 to 90 per cent of all hemolytic blood transfusions can be explained by Rh incompatability.

In obstetrics, the infant mortality due to erythroblastosis or hemolytic anemia of the newborn can be decreased by utilizing the information acquired from the routine Rh typing of all obstetric cases. This information forewarns us of the possibilities and probabilities of hemolytic anemia in the newborn, so that appropriate safeguards may be taken, and we may be prepared to interfere at the proper time with early induction of labor, or with immediate blood transfusions.

It is generally agreed<sup>5</sup> that erythroblastosis in the first born of Rh-negative women usually does not occur, i.e., one or more pregnancies with an Rh-positive fetus are necessary to produce isoimmunization of a sufficient intensity to produce hemolytic anemia in the next Rh-positive infant. The exceptions to this are in cases of Rh-negative women who have been previously immunized by transfusions of Rh-positive blood. The first born of these latter women may have erythroblastosis.

My personal management in the following series of 300 cases was as follows:

1. Every pregnant woman has a specimen of blood taken for the Rh factor and blood group determination at her first or second prenatal visit. The blood for the required Hinton test is obtained at the same time.

2. If the patient is Rh positive, nothing further is done in so far as her blood factor is concerned, since we know that complications may arise only in the Rh-negative women who have Rh-positive fetuses. There is one exception

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### Summary

From the experience of delivering three hundred patients by cesarean section under continuous spinal analgesia with no maternal deaths, we feel that it is a safe anesthetic for both mother and child. All of the babies (excepting the stillborn) showed no anoxemia, cried at once, were a good color, and required no resuscitation.

The postoperative morbidity of the mother was low, and the complications were no greater than with inhalation anesthetics.

The advantages of continuous spinal analgesia with its safety, low dosage, and controllability are emphasized and should make its use desirable in cesarean section.

The technique is easy and requires only the care and caution that should be given when administering any anesthetic.

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### Discussion

DR. CLIFFORD B. LULL.—I can remember the time when I was one of the most vehement objectors to the use of spinal anesthesia in cesarean section. I have always admired Doctor Cosgrove of Jersey City who persisted in its use during all these years. The history of anesthesia for cesarean section at the Lying-In Hospital shows that for the last twenty-five years an endeavor has been made to get away from general anesthesia in these cases. We used the one-dose spinal, but after seeing the report of several deaths many years ago, we discontinued its use. During the years that followed, we did as many of our cesarean sections as possible under local anesthesia. The rest of our cases were done mainly under nitrous oxide and oxygen. Following the development of fractional spinal by Dr. Lemmon, we went back to the use of spinal anesthesia in our cesarean section cases and have had excellent results. I believe this can be attributed to three factors: The control by the fractional method, the use of much smaller doses, and the availability of drugs of much less toxicity. After using continuous caudal analgesia for our vaginal deliveries, we began doing our cesareans under this type of pain relief. In addition to the series that Doctor Ullery reports here, we have performed more than 200 cesarean sections under continuous caudal anesthesia, and we have endeavored to evaluate, during the past three years, whether there is any difference in caudal, fractional spinal, and local anesthetics. We are of the opinion that fractional spinal is unquestionably the anesthetic of choice, although the difference between caudal and spinal is very slight, particularly as far as the convalescence of the patient is concerned. It takes longer for the proper level to be obtained under caudal, which increases the length of time spent in the operating theater. The benefits of these types of anesthesia have been very aptly discussed in the summary of Doctor Ullery's paper and I would particularly impress upon you the fact that we have had no trouble with the babies. The only ones who needed attention particularly were the ones who took a breath before they were extracted from the uterus. The second important fact is the uterine contraction, which occurs immediately, and the distinct decrease in blood loss. The convalescence of these patients is extremely smooth as they are able to partake of food within a short time after the operation is performed, and many patients who have had previous sections under general anesthesia will say that they felt much better on the first postoperative day than they did on the fourth or fifth day after their first cesarean operation. From our experience we believe that the use of general anesthesia in cesarean section will be limited to certain selected cases, or where trained anesthetists are not available to give the other types of anesthesia.

which the babies developed a slight amount of jaundice, although the blood picture was normal. Only two of these three mothers whose babies were jaundiced showed an appreciable amount of anti-Rh agglutinins in their blood after the seventh month. Labor was induced before term in both cases, and only one of these mothers gave birth to a true erythroblastotic fetus. That fetus was given five transfusions of Rh-negative blood and is now alive and well.

In this same group of 15 cases, seven were primiparas, seven were secundipara, and one was a tertipara. Assuming that with rare exceptions, as noted above, primigravidas do not develop erythroblastotic babies, we found only eight women who had the factors for potential erythroblastosis in the infant, and only one gave birth to a true erythroblastotic baby.

CASE 1.—Mrs. A. G., aged 31 years, gravida ii, para ii, Group O, Rh negative; husband Group O, Rh positive. First baby 4 years old, normal. Second pregnancy: normal prenatal course except for slight trace of albumin at last two prenatal visits. Blood pressure: systolic 120, diastolic 70. At eight months anti-Rh agglutinins were found in the mother's blood. Labor was induced three weeks from term. A male child weighing 7 pounds, 4 ounces was delivered normally. Shortly after birth he showed minimal evidence of erythroblastosis in that he appeared slightly edematous and had an enlarged liver. A few hours later jaundice was present and edema was more pronounced. A transfusion with 75 c.c. of Group O, Rh-negative blood was given immediately. The next day the red blood count was 5.1 and hemoglobin 94 per cent, with many nucleated red blood cells on smear. On the second day the red blood count dropped to 3.85, with 86 per cent hemoglobin; and another transfusion of 75 c.c. was administered. On the third day a third transfusion of 50 c.c. was given. On the fourth day blood examination showed his red blood count to be 6.1, with 122 per cent hemoglobin. On the fifth day there was a slight drop to 4.6 red blood count and 109 per cent hemoglobin. The blood picture stayed at about that level until the third week, when the blood began to drop and reached a low level of 2.4 red blood count, 44 per cent hemoglobin, with 2.7 per cent reticulocytes. During this third week the jaundice increased. At this time the fourth transfusion was given with marked improvement, and two days later a fifth transfusion was given, which was followed by a striking improvement in the infant's general condition. He was discharged home improved at the age of one month. He is now 10 months old and is progressing normally.

CASE 2.—Mrs. F. G., aged 30 years, gravida iii, para ii, Rh negative, Group A, husband Rh positive, Group A. Her first pregnancy terminated in a miscarriage at two months (January, 1942). Her second pregnancy went to term and she was delivered of a normal male child (May, 1943). In her third pregnancy she showed anti-Rh agglutinins in her blood at the eighth month. Labor was induced two weeks from term, and she was delivered normally of a male child on April 2, 1945. The baby was Rh positive and developed a slight amount of jaundice on the first postpartum day. Examination of the blood was normal. The jaundice subsided in a few days, and the baby's blood continued to remain within normal limits. Since there was no evidence of hemolytic anemia, no transfusions were administered. The birth weight was 6 pounds, 2 ounces. The baby was discharged well on the tenth day, weighing 5 pounds, 14 ounces with a normal blood picture.

### Summary

1. The Rh factor in obstetrics is discussed.
2. Every obstetric patient should have an Rh determination during her prenatal course.

to this, as has been shown by Wiener<sup>8</sup> and Diamond,<sup>1</sup> in cases where we have subtypes of Rh (Rh<sub>1</sub> or Rh<sub>2</sub>); here the mother, although Rh positive, may develop agglutinins against the Rh fraction which is foreign to her, and later under a similar set of conditions may develop transfusion reactions or may give birth to erythroblastotic infants. These cases are extremely rare.

3. If the mother is Rh negative, then an Rh determination is made from the husband's blood, and if he is Rh negative, there can be no incompatibility, and no further tests are performed.

4. If, on the other hand, the mother is Rh negative and the father Rh positive, we have the factors for possible hemolytic anemia or erythroblastosis. In these cases we test the mother's blood for anti-Rh agglutinins at the seventh month. If no appreciable agglutinins are found at this time we may assume that there will be no trouble, and may allow this patient to go to term. After delivery, the baby's blood is examined for anemia and the Rh factor. If the baby is Rh negative, then we know that the father is a heterozygous Rh positive, and his offspring may be Rh positive or Rh negative. If the baby is Rh positive then we know that the father may be either homozygous or heterozygous Rh positive. A further test on the father's blood will determine into which group he belongs.

5. When anti-Rh agglutinins are found in the mother's blood at the seventh month, we check her titer every two weeks and, if there is no increase in the anti-Rh agglutinins, we allow the patient to complete eight full months of pregnancy and, if we feel that the baby is large enough to have a good chance for survival, we induce labor at this time. If there is a marked increase in the titer we weigh the various possibilities and may induce labor one week before eight full months of pregnancy. We do not feel that it is advisable to induce labor earlier than that, because the baby is usually too premature to survive.

6. After these babies are delivered, we examine the baby thoroughly for evidence of erythroblastosis, and do an Rh factor and complete blood examination. If the infant shows evidence of hemolytic anemia, the child is transfused with Rh-negative compatible blood. A complete blood examination is performed daily and, if hemolysis is still going on, more transfusions are administered until the baby's blood is normal, or the hemolysis has stopped. If this is done, many of the erythroblastotic babies will be saved.

7. We do not allow breast nursing in erythroblastotic infants because anti-Rh agglutinins may be secreted in the milk and, after absorption through the stomach, may produce further hemolysis of the infant's Rh positive cells.<sup>1, 8, 9</sup>

In a series of 300 consecutive personal deliveries, there were 32 Rh-negative mothers. The remaining 268 were Rh positive; therefore, approximately one out of every nine mothers was Rh negative. This is what one would expect in the general white population.

Examination of the husband's blood of these 32 Rh-negative mothers revealed the following: 22 Rh positive, and six Rh negative. The blood of the remaining four husbands was not obtained because they were serving in the Armed Forces and were overseas.

In the matings of the 22 Rh-positive husbands with the Rh-negative mothers, the infants were Rh positive in 15 cases and Rh negative in seven. In this series, at least seven out of the 22 Rh positive fathers were heterozygous.

Of the 15 cases in which the factors for potential erythroblastosis were present, that is, an Rh-negative mother, with an Rh-positive father and an Rh-positive fetus, there was only one case of true erythroblastosis, and two cases in



## THE KIELLAND FORCEPS FOR USE IN THE OCCIPITOPOSTERIOR AND OCCIPITOTRANSVERSE POSITIONS\*

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IN A recent paper on occipitoposterior position, Hennessy<sup>1</sup> stated: "The occipitoposterior position is perhaps the most common and important abnormality in the mechanism of vertex presentations. Its management has long been a matter of discussion. Although the literature on the subject is voluminous, there will undoubtedly be many more contributions, for there will always be a posterior."

The occipitoposterior position is probably much more common than is generally supposed. The reported incidence varies greatly: Tweedy and Wrench<sup>2</sup> reported 121 cases in 15,167 deliveries (0.8 per cent); Williams,<sup>3</sup> 11.3 per cent in 5,000 cases; Scott,<sup>4</sup> 14.04 per cent in 1,000 consecutive cases; Piper,<sup>5</sup> 17.1 per cent; and Danforth,<sup>6</sup> 25.1 per cent in 1,131 private deliveries. D'Esopo<sup>7</sup> noted that 19 per cent of all vertex presentations engaged in the posterior position.

In 1915, Christian Kielland of Norway presented a new type of forceps before the Munie Gynecological Society. Greenhill,<sup>8</sup> in 1924, summarized 36 statistical reports concerning the use of the Kielland forceps in 1,762 deliveries. Most of the authors agreed that the instrument was a definite advance for delivering babies when the occiput is not in the anterior half of the pelvis. Jarcho<sup>9</sup> has by diagram demonstrated satisfactorily the use of the instrument.

Briefly, this instrument is very light, with a very slight pelvic curve, a sliding lock, and a small knob attached to each handle. Before the instrument is applied, it is placed in front of the patient with the concave margins of the blades toward the occiput. The anterior blade is introduced first. The blade is introduced between the cervix and the head, with the cephalic surface of the blade facing upward. It is pushed up gently until the entire blade is completely above the symphysis pubis and the shank lies in the subpubic angle. At this time the blade is rotated on its own axis in the direction of the knob. This rotation caused the cephalic surface of the blade to lie on the baby's head. The posterior blade is then introduced in the same fashion as one would for an occiput anterior. Occasionally, the posterior blade will not enter easily because it encounters the anterior surface of the sacrum. This can be corrected by depressing the handle of the blade, causing its tip to hug the occiput and, under guidance of the hand in the vagina, application is completed. After the blades are locked, traction is applied in the direction in which the handles point until the head enters the largest diameter of the pelvis. At this point the forceps are rotated gently on the long axis without traction until the small fontanel reaches the subpubic region. When the mueha impinges under the symphysis

\*Presented before the Bronx Gynecological and Obstetrical Society, Nov. 26, 1945.

3. When anti-Rh agglutinins are present, labor should be induced before term.
4. Erythroblastotic babies with hemolytic anemia should be treated with immediate transfusions.
5. Transfusions reduce the mortality in erythroblastosis fetalis.
6. Three hundred consecutive deliveries are analyzed. In this group two women had anti-Rh agglutinins present and had labor induced before term. One of these infants had true erythroblastosis fetalis and, with five blood transfusions, survived and is alive and well.
7. The incidence of erythroblastosis fetalis in this series was 1 in 300.

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The indications for the termination of labor were strict. Full dilatation for two hours or more without progress was the indication in 112 cases (56 per cent). In 77 cases (33 $\frac{1}{3}$  per cent), the indication was fetal distress with full dilatation, except as noted below. Of course, in these cases the two hours of second stage labor was waived. Fetal distress was denoted not alone by the passage of meconium, but by the combination of a rising or falling fetal heart rate in addition to the passage of meconium. Among these 77 patients, there were six primigravidas who developed fetal distress when not quite fully dilated. In each case it was felt that the cervix was dilatable. Dührssen's incisions were performed before the application of the forceps. Living babies resulted in all cases. The mothers' puerperia were uneventful.

There were six cases of compensated mitral stenosis, where the second stage was entirely eliminated. Forceps were applied when full dilatation was attained.

### Type of Laceration

There was no laceration in 20 patients (10 per cent) of the cases in this series.

The third degree lacerations, five in number, occurred in primigravidas. Healing took place by primary intention following immediate repair of the pelvic floor and anal sphincter. It was felt that in each case the laceration was sustained because the concurrent episiotomy was not of sufficient length.

In 10 cases there was a cervical laceration requiring repair. Of these, in six cases Dührssen's incisions were the cause of the laceration. In the other four cases inspection of the cervix following the delivery revealed unilateral lacerations because of bleeding not due to a relaxed uterus. These were immediately sutured. There was no subsequent morbidity in the mother.

### Maternal Mortality and Morbidity

A patient having a temperature of 100.4° F. on two occasions, excluding the first postpartum day, was considered a morbidity. There were 42 cases, or 21 per cent, with morbidity. Their causes are noted in Table II.

TABLE II. MORBIDITY

CAUSE	NUMBER OF CASES
Pyelitis	3
Infected episiotomy	2
Uterine infection	24
Nonsuppurative mastitis	1
Parotitis	1
Aspiration pneumonia	1
Undetermined	10

There was one maternal death:

CASE 1.—(Hosp. No. 22081.) A 29-year-old primigravida who had ample pelvic measurements. After a seventy-two-hour labor with a two-hour second stage, the head was arrested in left occipitoposterior position. The Kielland forceps was applied and the head was delivered with moderate difficulty. The baby weighed 7 pounds, 14 ounces, and was in good condition. Bleeding occasioned by a left cervical laceration was controlled by a repair. A laceration through the posterior vaginal wall, extending into the rectum, was repaired. The sphincter was not injured. The patient was given a 750 c.c. clysis of saline solution. She was returned to her room in good condition and reacted well until the third day post partum. At this time she complained of a painful swelling of the left vulval region. On examination a huge hematoma was noted. She was immediately removed to the operating room for transfusion and operation. Before these procedures were begun she suddenly expired. No doubt

pubis, the forceps are removed and delivery completed in the usual way. The application of the forceps for the occipitotransverse position is essentially the same.

### Record of Cases

We wish to report 200 consecutive occipitoposterior or occipitotransverse positions delivered by mid-Kielland forceps at The Bronx Hospital. These patients were delivered by different physicians on the private and ward services. Many of the cases were delivered by the house obstetricians under the supervision of one of the visiting staff physicians. In all of the cases, the pelvis was clinically ample and the vertex was engaged at the time of delivery. We do not advocate the use of high forceps at any time, preferring (1) a version when version is not contraindicated, or (2) a cesarean section where there is cephalopelvic disproportion.

In the beginning, it was felt that lacerations of the pelvic floor were more extensive when the Kielland forceps was used for extraction as well as rotation. Therefore, on 23 occasions the Kielland forceps was used for rotation, and the Elliott or Dewees forceps for the extraction. Experience has disproved this assumption.

TABLE I

PARITY					POSITION OF VERTEX AT TIME OF DELIVERY				INDICATIONS FOR TERMINATION OF LABOR				TYPE OF LACERATION				
PRIMI GRAVIDA	GRAVIDA II; PARA I	GRAVIDA III; PARA II	GRAVIDA IV; PARA III	GRAVIDA VI; PARA V	LEFT OCCIPITOPOSTERIOR	RIGHT OCCIPITOPOSTERIOR	LEFT OCCIPITOTRANSVERSE	RIGHT OCCIPITOTRANSVERSE	PERSISTENT OCCIPITOPOSTERIOR OR OCCIPITOTRANSVERSE WITHOUT PROGRESS	PERSISTENT OCCIPITOPOSTERIOR OR OCCIPITO-TRANSVERSE WITH FETAL DISTRESS	PERSISTENT OCCIPITOPOSTERIOR CARDIAC; FULLY DILATED	LACERATION OF CERVIX REQUIRING REPAIR	DÜHRSSSEN'S INCISIONS	FIRST DEGREE OF PERINEUM	SECOND DEGREE OF PERINEUM	THIRD DEGREE OF PERINEUM	EPISIOTOMY
160*	23	14	1	2	49	98	37	16	117	77†	6	10‡	6‡	22	27	5	110

\*This included four cases of gravida iv; para 0, and 9 cases of gravida ii; para 0. (All essential primigravidas.)

†In 6 of these cases there was not quite full dilatation. Dührssen's incisions were used before the application of the Kielland forceps. An episiotomy was also performed.

‡All 10 cases also had an episiotomy. The six cases of Dührssen's incisions are included in this total.

### Indications for Termination of Labor

In this series of cases (Table I), 80 per cent (160 patients) were primigravidas. Among the multiparas, there were ten who had had a Kielland forceps delivery with their first baby. The most common position was right occipitoposterior, occurring 98 times; i.e., 44 per cent of the cases.

strument. Bladders have been torn with the ordinary obstetric forceps when improperly used by inexperienced operators. Everything else being equal, the instrument is as good as the obstetrician who wields it.

In the series of cases here presented, we feel sure that the more serious injuries obtained could have been avoided to a great extent, or at least minimized, had the particular operators been better acquainted with the instrument, and more liberal with episiotomy.

### Summary

1. Two hundred cases of persistent occipitoposterior or occipitotransverse positions delivered with the Kielland forceps are analyzed.
2. There was one maternal death.
3. There were 14 fetal and neonatal deaths. In six cases the fetal heart was lost before the forceps were applied. The corrected fetal mortality was 4 per cent.
4. The advantages of the Kielland forceps are discussed.

### Conclusions

1. The dangers attributed to the Kielland forceps by other reports have no basis of fact.
2. The Kielland forceps comes nearer to being the universal method of choice for the treatment of persistent occipitoposterior or occipitotransverse position.
3. Under proper supervision the use of this instrument can be easily learned by any one who has had a proper obstetrical training.

We wish to express our appreciation to Dr. Meyer Rosensohn for his interest and stimulating advice in the preparation of this report. We are grateful to Comdr. Abraham J. Fleischer, U.S.N.R., and Dr. Jacob Clair for aid in the preliminary studies.

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1840 GRAND CONCOURSE  
1229 CLAY AVENUE

this internal hemorrhage had been growing for some time, but was not noticed until it had reached a lethal limit. Closer observation of this patient in her puerperium might have resulted in earlier recognition of the condition, with a strong possibility of avoiding this calamity.

### Fetal Mortality

In this series of cases there were 11 stillbirths and three neonatal deaths, a percentage of 7 per cent. Six of the stillbirths occurred in patients with prolonged labors where the fetal heart was lost before the forceps application, making a corrected fetal mortality of 4 per cent. In three other cases difficulty was experienced with the delivery of the shoulders resulting in stillbirths. In the remaining two cases no obstetric reason for the stillbirth could be determined. All of the 11 cases showed cerebral hemorrhage at necropsy.

The three neonatal deaths also showed cerebral hemorrhage at autopsy.

### Discussion

The Kielland forceps is not a panacea for all occipitoposterior or occipitotransverse deliveries. In the hands of those well versed in the mechanics of the instrument, it comes nearer to being the universal method of choice than any other procedure. Manual rotation of the head followed by forceps application for extraction very frequently is a failure because of the difficulty in keeping the head in the anterior position while applying the blades. In addition, not infrequently the head is dislodged during this procedure. In the Pomeroy maneuver it is necessary to disengage the head in order to be able to rotate the shoulders. This method again entails the disadvantage of entering the uterus, with the possibilities of infection, in addition to the ever-present danger of prolapsing the cord. The Scanzoni maneuver, no doubt an excellent procedure in good hands, has the disadvantage of the necessity of multiple applications. Frequently, rotation is difficult because of the large pelvic curve of the ordinary forceps (Simpson, Elliot, Tucker-McLane). This necessitates rotation through a comparatively large arc, and no matter how careful the operator is in describing the small arc with the tips of the blades by rotating the handles through a large arc, the attendant injuries of the soft parts as a result of this procedure is an ever-present danger.

With the Kielland forceps the disadvantages of the other maneuvers are overcome. Once applied, rotation through a small arc is possible without reapplication, and with a minimum potentiality for injuries to the soft parts. In other words, rotation and extraction are accomplished with only one application. The hazards that are attributed to the introduction of the anterior blade of the Kielland forceps really do not exist when the instrument is properly applied. We have never seen a rupture of the bladder in our cases. The cases of vesicovaginal fistulae resulting from the use of the Kielland forceps reported in the literature can be attributed to two possible causes. The first, devitalization of the vesicovaginal septum resulting from the incessant pounding which it suffers from the head in a prolonged labor. Such a condition is occasionally encountered in normal spontaneous deliveries. The second, and more important, explanation for bladder injuries with the use of the Kielland forceps must be looked for in the shortcomings of the operator rather than in those of the in-

abnormalities. The blood pressure was 125/80, the urine normal (no sugar). There was a polycythemia of 5,480,000, hemoglobin 13.5 Gm., the differential count normal.

Surgical exploration of the abdomen revealed an orange-yellow, small, rather firm tumor in an otherwise apparently normal right ovary. The ovary was removed. The other internal genitals were of normal appearance, except that the left ovary was of notably small size.



Fig. 1.—Adrenal-like tumor of ovary, case 3878. Actual size of one-half of ovary with one-half of tumor. The surface of the tumor appears rounded because the specimen was bisected before fixation. The growth was of distinctly yellow color and of firm consistency.



Fig. 2.—Adrenal-like tumor of ovary, case 3878. Specimen has been cut at right angle to surface shown in Fig. 1. Grossly, the growth is similar to a corpus luteum, but it is more firm, more definitely a tumor surrounded by a crescent of ovarian tissue. ( $\times 2\frac{1}{2}$ .)

Menstruation began two months after operation and continued regularly and normally, four days in duration, until the patient became pregnant at the end of one year. Gestation terminated in premature birth of a female child who lived only one hour. When last seen, just prior to the labor, there had been no notable change in the hypertrichosis, and the voice was still somewhat husky. The aene had improved, and the clitoris had returned to normal.

The tumorous right ovary, bisected immediately after removal, consisted of an orange-yellow tumor, which comprised approximately two-thirds of the

## THE ORIGIN OF ADRENAL-LIKE TUMOR OF THE OVARY\*

(Hypernephroma of Ovary, Adrenal Tumor of Ovary,  
Masculinovoblastoma, Luteoma, Luteinoma)

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ASIDE from arrhenoblastoma, masculinization may also be produced by an adrenal-like tumor of the ovary. Only 15 well-authenticated cases of this rare growth have been reported in the literature, not including the one herewith presented. Despite its rarity, all should be conversant with the characteristics of this unusual kind of masculinizing tumor, for knowledge of it has a direct bearing on our understanding of other ovarian neoplasms.

The adrenal-like tumors thus far described have been remarkably similar. All but one have been unilateral. Although ranging from microscopic to orange size, nearly all have been small nodules not larger than a walnut. Most of the growth is usually buried in the ovary, sometimes protruding from the surface, but always covered by at least a thin layer of ovarian tissue. The color has been invariably yellow except in one case; a distinct orange-yellow is the predominant color. All of these tumors are solid, rubbery, and ovoid. Usually the growth is lobulated by fibrous septa which radiate from the capsule.

Microscopically, the tumor is composed of large, polyhedral, eosinophilic cells disposed in cords, nests, and anastomosing strands. They fill in the spaces of a network formed by capillaries branching out from scattered larger vessels. Stroma is usually scanty. The cells have distinct outlines and a granular protoplasm; the nuclei are chromatic rather than vesicular; nucleoli are invariably present. Considerable lipoid material is usually to be seen.

All authentic adrenal-like tumors of the ovary present symptoms of masculinization. Amenorrhea, hirsutism, and hypertrophy of the clitoris always occur and are indistinguishable from similar disturbances characteristic of arrhenoblastoma. In addition, some of the reported cases of adrenal-like tumor had glycosuria, polycythemia, and hypertension; these are equally suggestive of adrenal cortical disturbances or tumor or basophilic adenoma of the pituitary gland, but they do not usually occur with arrhenoblastoma.

### Case Report

L. C., No. 3878, a patient 23 years of age, operated upon June 15, 1943, by Warner S. Bump, complained of infertility, amenorrhea for six years, acne of the shoulders, marked growth of hair, and a lowered pitch of the voice.

Examination revealed marked universal hypertrichosis of the body surfaces. The clitoris was greatly enlarged. Pelvic palpation, x-ray examination of the skull, and air insufflation of the perirenal tissues failed to disclose other

\*Read before the Chicago Gynecological Society, November 16, 1945.



stromatogenous pattern. In many areas of the tumor there is a clearly defined transition from the adrenal-like polygonal epithelioid type of cells to the spindle-shaped type of cells.

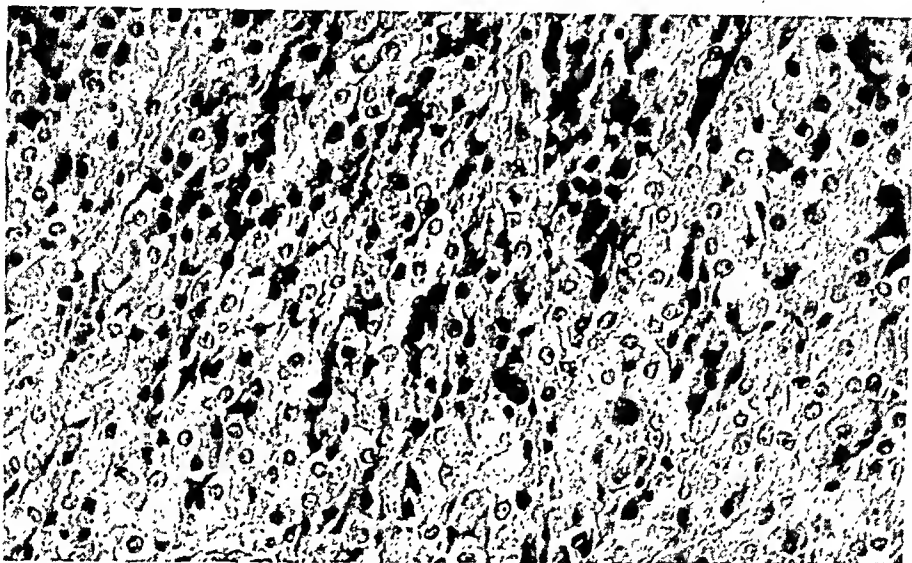


Fig. 4.—Adrenal-like tumor of ovary, case 3878. Dark cells, containing much pigment, and light cells, almost devoid of granules, are comparable with kindred cells of the adrenal cortex. ( $\times 270$ .)

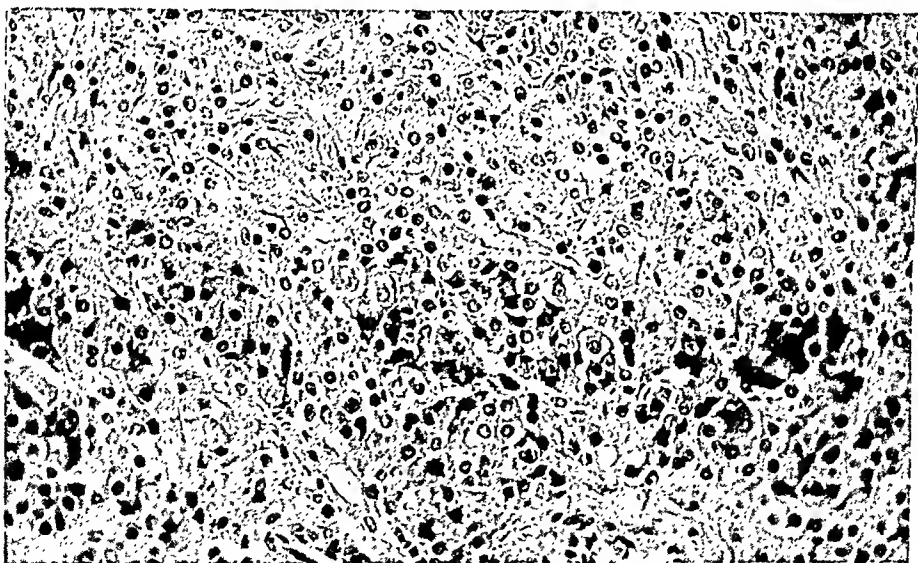


Fig. 5.—Adrenal-like tumor of ovary, case 3878. Note the gradual transition from polygonal cells to a more stromatogenous type. ( $\times 205$ .)

Fat is present in considerable amount, chiefly intracellular. Some is in the form of larger particles, but much more is in fine granules. Most fat is found in necrotic areas (which are a feature of this tumor); a considerable amount is present in the light staining cells, little in the dark cells.

Although, grossly, the tumor has a rather definite capsule and appears delimited from the ovarian tissue, microscopically the transition is often not clearly demarcated, and a richly cellular, often hyalinized capsule of greatly

ovary, surrounded by a gray crescent of firm ovarian tissue. Toward the hilus the ovarian tissue was represented mostly by the tumor capsule, there being very little ovarian tissue overlying the capsule; even here, there was no prominence on the surface of the ovary.

The entire bisected specimen, after prolonged fixation (Fig. 1), was 3 by 2.7 cm. on the surface and 0.8 cm. in thickness (representing one-half of the thickness of the entire specimen). The tumor was buried in the ovarian tissue, and protruded disc like from it, 2 by 1.8 cm. in surface measurements. The tumor surface was granularly smooth, in gross appearance resembling adrenal tissue or a tumor of the corpus luteum.

When cut at right angles to the position shown in Fig. 1, the slightly magnified gross specimen is seen to be lobulated by fibrous septa which radiate from the capsule (Fig. 2).

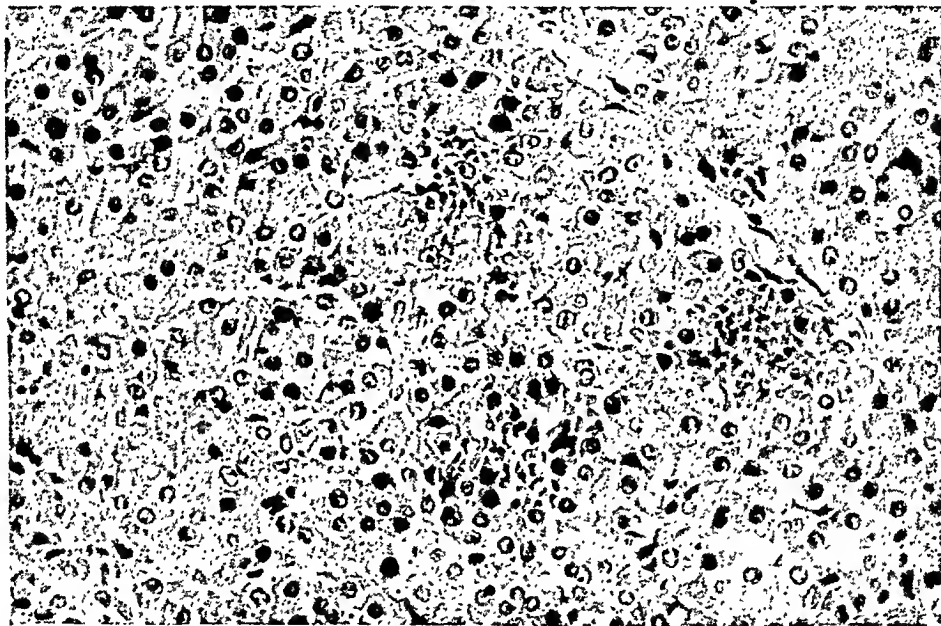


Fig. 3.—Adrenal-like tumor of ovary, case 3878. Clusters of polyhedral cells arranged in acini. Note the rich sinusoidal blood supply. ( $\times 270$ .)

Microscopic examination reveals massive strands, wedge-shaped areas, and isolated clusters of cells arranged in acini, also cord-like patterns and anastomosing networks, like the zona fasciculata and the zona reticularis of the adrenal cortex. All of these are polygonal cells, provided with a rich sinusoidal blood supply. The individual cells are clearly demarcated and lie in close apposition. The nuclei are sharply outlined, chromatic, the nucleoli small, deeply staining, eccentrically placed. The cells of this group, similar in outline and in nuclear characteristics, differ greatly in staining reaction, some dark and containing much pigment, others much lighter and almost devoid of granules in the protoplasm, although the nuclei are distinctly granular (Fig. 4).

Other lightly staining cells constitute the more stroma-like, greater bulk of the tumor. Here the blood supply is scanty. The tissue still preserves a richly cellular character, composed of more spindle-shaped cells in a loosely woven pattern. The cell boundaries are less clearly defined than those of the previously described adrenal-like cells, and are provided with a fine collagenous network of intercellular fibrils (Fig. 6). The nuclei are more ovoid and darker, manifesting a tendency to deviate, together with the stroma, into a

In contrast with the ease of identification of this tumor, knowledge of its origin has remained a puzzle. It has been the consensus that a decision relative to the genesis and nature of the growth is unwarranted on the basis of evidence thus far accumulated. A teratomatous derivation is admitted as a theoretical possibility, but has been relegated to a position of secondary importance. The possibility of corpus luteum origin or of development from adrenal rests in the ovary has brought forth much speculation and many interesting discussions. Because the corpus luteum is a highly specialized evanescent glandular structure, Miller and Meyer dismiss the thought of a tumor originating from it. Schiller, in speaking against a lutein cell origin, says that a luteoma, in order to be of theca lutein or granulosa lutein origin, must be of connective tissue type, whereas the type of tumor under consideration is comprised of epithelial cells. He states further that as long as granulosa cells are not luteinized they show their mesenchymatous origin by connections with the protoplasm of syncytial cells, but that all luteomas thus far described show no such cell-connecting fibers.

Saphir and Laekner demonstrated that there are two kinds of yellow ovarian tumors which resemble each other. One is the masculinizing tumor under present consideration. The other is a nonmasculinizing hypernephroid carcinoma; it evidently arises from intraovarian mesonephric or teratomatous rests, and is similar to hypernephroid carcinoma of the kidney. This hypernephroid clear-cell adenocarcinoma of the ovary is microscopically quite different from the tumor we have been considering, does not arise from suprarenal cortical tissue, and evidently accounts for many of the growths which have long been recorded in the literature as hypernephroma of the ovary.

It is worthy of note that only the malignant cortical tumors of the suprarenal gland produce virilism. In contrast, adrenal-like tumors of the ovary are nearly all benign (potentially malignant), suggesting some other origin. Also, if adrenal rests do give rise to adrenal-like tumors of the ovary it is strange that adrenal rests are rarely, if ever, demonstrable in the ovary. Those reported are usually confused with corpora atretica (Miller).

Zwemer, Wotton, and Norkus demonstrated that in the adrenal gland new glandular cells of the adrenal cortex are derived from indifferent cells of the capsule. The process occurs by growth inward from fibroblast-like previously undifferentiated cells of the capsule which undergo morphogenesis during migration. A gradual progress inward of the adrenal cortex cells, comparable with the slow movement of a viscous fluid, has already been noted by many other observers.

In a study of adrenalectomized ground squirrels sacrificed from three days to one year after adrenalectomy, Groat demonstrated extensive growth of adrenocortical-like cells in the ovaries. The process was demonstrated to be a metaplasia of stroma cells of the ovary and mesenchyme-like cells in the mesovarium into an epithelial type of cell. In one animal, one hundred and eighteen days after adrenalectomy, the medulla of the ovary was solidly filled with this adrenal-like tissue, there were clumps in the cortex, and one large body extended from the mesovarium into the ovary.

varied thickness gradually merges in many places into the ovarian stroma. In the ovary, some ova are seen. There are some larger follicles with marked luteinization of both granulosa and theca. The stroma is richly cellular, consisting of actively proliferating spindle cells with a tendency to formation of a basket weave and differentiation in an epithelial direction. Whatever has stimulated the tumor growth has evidently had a similar activating influence on the ovarian stroma.

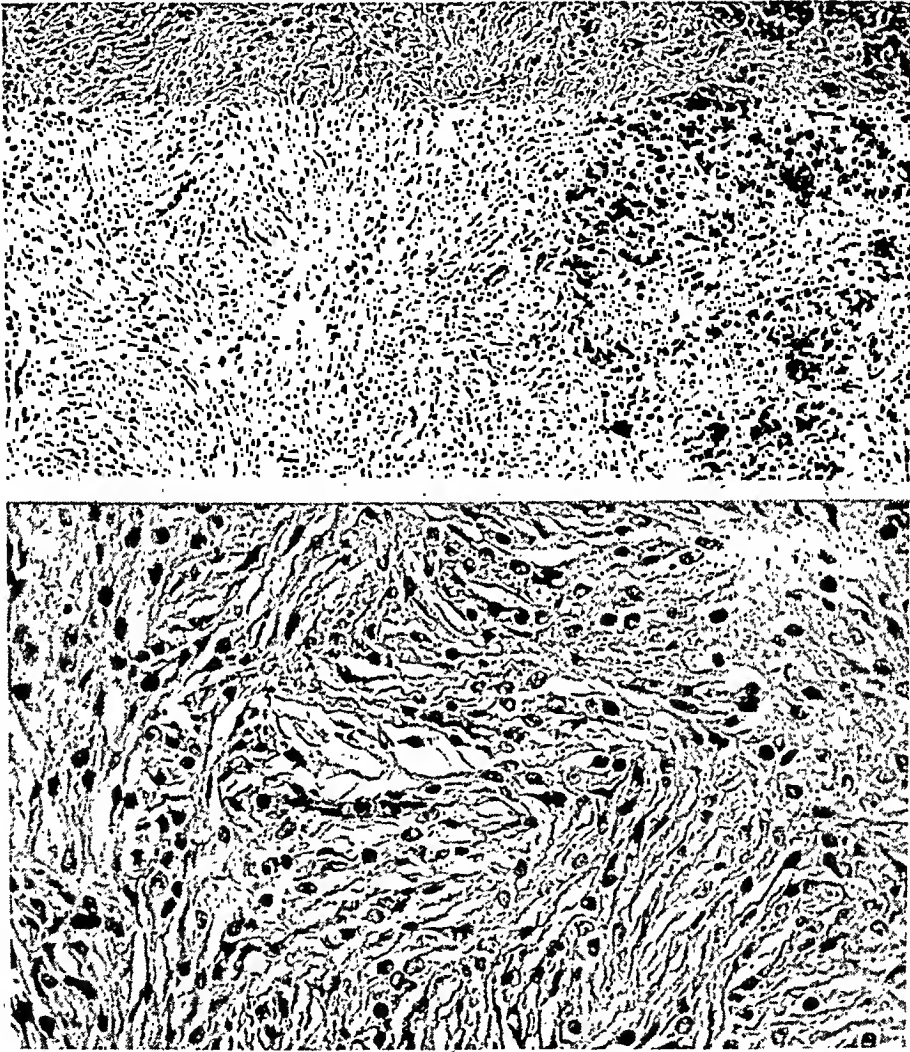


Fig. 6.—Adrenal-like tumor of ovary, case 3878. A. There is gradual transition from a polygonal adrenal type of cells on the right to a stroma composed of spindle-shaped cells on the left. ( $\times 95$ .) B. Higher magnification of the field shown above on the left, revealing finer details of the cellular pattern—a thecoma-like basket weave of stroma cells provided with a network of intercellular fibrils. ( $\times 270$ .)

### Discussion

The pathologic diagnosis of an adrenal-like tumor of the ovary is relatively simple if study of the growth is aided by a history of masculinization. The latter is essential; without it a positive diagnosis is unwarranted, irrespective of the gross and microscopic evidence. Postoperative recession of symptoms and gradual resumption of normal physiologic activity confirms the diagnosis.

From the accumulated facts now available, it seems that no distinction should be made between adrenal-like tumor and luteoma or luteinoma of the ovary.

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303 EAST SUPERIOR STREET

### Discussion

DR. JOHN BREWER.—I should like to limit my remarks to the masculinizing tumor that Dr. Curtis has presented under the title "Adrenal-like Tumor of the Ovary." The primary objective of the presentation, which Dr. Curtis so ably made, is to demonstrate the origin of this type of masculinizing tumor. Many theories have been offered in the past and there has been much speculation, but no worker up to the present has given demonstrable proof concerning the origin.

The adrenal rest theory has certain deficiencies: (1) adrenal rests are not found within the ovary itself, and (2) transitional stages from adrenal rest tissue to this type of tumor tissues have not been shown.

The photomicrographs of transitional stages between stromal cells of the tumor and the epithelial-like cells comprising the tumor give conclusive evidence that this tumor arises from cells of the ovarian stroma. As far as I know, this is the first such demonstration. From the evidence we must accept the fact that this tumor arises from ovarian stromal cells.

With the origin of this type of tumor established, follow-up study and work will in the near future bring out all the salient features of this particular masculinizing ovarian tumor. The great confusion in nomenclature will be clarified and a single generally accepted name will evolve. Such fundamental work as this which has been presented is absolutely necessary as a basis upon which other facts can be built, and this eventually will enable us to reach a final and true understanding of an ovarian tumor which for a long time has remained obscure.

DR. CURTIS (Closing).—It is apparently evident, after study of this tumor, that it arose from metaplasia of stroma cells, or other indifferent cells of the ovary. There is no need to complicate the problem by assuming that the growth had its inception in embryonic rests: nor is there evidence that this was a preformed tumor which later became luteinized; discussion of luteinization serves merely to confuse the issue.

Granted that we have produced evidence that a tumor has been developed by metaplasia of normal cells, a really decided step forward has been made. Surely, other types of tumors may have similar origin from stimulation of apparently indifferent tissue cells. Discussion of the nature of such stimulation is not warranted without further evidence.

Let us summarize the available evidence concerning the nature of an adrenal-like tumor.

The fact that adrenal rests in the ovary are exceedingly rare at once makes questionable such origin of adrenal-like tumors. It becomes even more doubtful when we note that only malignant tumors of the suprarenal gland produce virilism, whereas adrenal-like tumors of the ovary are essentially benign.

Surely, there is no need here to discuss the theoretical possibility of luteinization in a pre-existent granulosa or theca-cell tumor in explanation of the origin of this masculinizing growth.

Authentic adrenal-like tumors of the ovary, so accurately described and discussed by Rottino and McGrath, and by Kepler, Doekerty, and Priestley, all seemingly develop within the substance of the ovary, as though produced by a perverted physiologic process, rather than originating as an independent growth. The capsule of an adrenal-like tumor is not a true capsule, but consists of a shell of ovarian tissue.

The assumption that a luteoma or adrenal-like tumor of the ovary is an epithelial growth originating from dormant cells and that it cannot arise from stromal tissue is contrary to the evidence of Zwemer, Wotton, and Norkus, who demonstrated that glandular cells of the adrenal cortex develop from fibroblast-like previously undifferentiated cells of the adrenal capsule. It is contrary, also, to Groat's experimental production of adrenocortical-like masses of cells from metaplasia of stroma cells or indifferent cells in the ovaries of adrenalectomized ground squirrels.

For the sake of greater clarity, let us quote from Maximow-Bloom:

"The interstitial connective tissue or stroma of the human ovarian cortex consists of a network of reticular fibers and spindle-shaped cells. . . . The cells of the ovarian stroma are probably not common fibroblasts, for they may give rise to interstitial cells. . . . Much has been written on the endocrine nature of the 'interstitial cells' of the ovary. . . . It is impossible to separate them experimentally from the other constituents of the ovary. . . . In the adult human ovary the interstitial cells are either absent, or present in small numbers as irregular cords of large polyhedral 'epithelioid' cells scattered in the stroma."

The inference is that interstitial cells may really be identical with ordinary ovarian stroma cells. In our case a direct sequence of transition from typical adrenal-like epithelioid cells to a spindle-shaped type of cells provided with intercellular fibers is clearly evident microscopically. It will be recalled that Schiller emphasized the importance of cell-connecting fibers in evidence that a tumor may be classified as of lutein origin, a feature characteristic of our tumor (Fig. 6), but not heretofore demonstrated in luteoma or adrenal-like tumor.

It would appear that adrenal-like tumor growths of the ovary arise by metaplasia of stroma cells or other indifferent cells rather than from embryologically misplaced tissue in the ovary. The growth is comprised of luteinized epithelioid and spindle shaped cells. Whether the cells which comprise the tumor are to be called epithelial is arbitrary.



*Pathologic Report.*—

*Gross description:* This slightly oval-shaped tumor measured  $9\frac{1}{2}$  by 8 by  $6\frac{1}{2}$  centimeters. It was smooth and quite regular. The color was a yellowish gray. The mass was quite firm, except over a very obvious cystic portion which occupied about two-fifths of the mass. This cystic portion of the tumor had a thin, tough wall opposite the solid portion of the tumor, and was filled with straw-colored clear fluid. The thin capsule which surrounded the entire tumor mass was apparently the remaining compressed ovarian tissue. The cut surface of the tumor was homogenous in appearance and of a light yellowish tan color. These surfaces remained smooth after cutting, except for some change in level between the coarse lobular divisions of the tumor. The solid portion of the tumor was flattened on the side of the cyst. Visible blood vessels were few except in the capsule which, as stated above, appeared to be a remnant of the ovary.



Fig. 1.—Moderately high power photomicrograph showing the irregular cords of cells which appear as tubules between which are more diffuse masses of similar cells and many less deeply stained masses of interstitial cells. Histologic diagnosis: Undifferentiated arrhenoblastoma of ovary.

*Microscopic description:* The epithelial arrangement of this tumor was less complicated than that of most of the tumors of this type. The only definite arrangement was in the form of zigzag cords of elongated cells which tended to extend at right angles to the direction of the cords. Right angle branching of these cords appeared to be a fairly characteristic feature. Narrow spaces appeared about these unit structures which ended in broad indistinct cords, which formed a network about areas of less deeply stained stroma where interstitial cells appeared. The stroma is quite vascular, and there was some suggestion that these blood vessels may have been continuous with the spaces about the cell cords. Nuclei were few in the stroma, except where interstitial cells were grouped. In some of the broader, more diffuse cords of epithelial cells there was the slightest suggestion of alveolar arrangement

# ARRHENOBLASTOMA OF THE OVARY\*

## Report of Two Cases

MARK T. GOLDSTINE, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, Northwestern University Medical School and Wesley Memorial Hospital)

CASE 1.—Mrs. V. N., aged 25 years, fair complexion, married five years, no children, no pregnancies.

Menstruation began at twelve years of age, was regular, 28-day type, and of five to six days' duration. There was some discomfort with the menstrual periods from the beginning, and this gradually increased in severity to the time where the pain was quite severe and required her leaving work for two or three days. At the age of twenty she noted that her menstrual periods were less in amount but of the same duration and interval. The dysmenorrhea became increasingly severe. At the age of 23 years her menstrual periods ceased and she had not menstruated for two years before coming for examination.

When the patient presented herself for examination the foremost complaint was dyspareunia, which was so severe that coitus was impossible for the last eight months. She attributed this to a growth between the labia which annoyed and irritated her at all times. The second complaint was voice change, which became so pronouncedly masculine that it necessitated her leaving the church choir. There had been a gain in weight of between 40 and 50 pounds in four years, and a growth of hair on face, arms, and legs. The failure to have children did not cause her much anxiety, and the amenorrhea was gratefully accepted because of the relief from menstrual pain. There was nothing remarkable in her childhood or adolescent history.

The general physical examination was negative. The breasts were large and pendulous. There was some regression of the areolae and nipples. Numerous follicles were present.

*Pelvic Examination.*—The external genitals were normal, except for enlargement of the clitoris which measured 7 cm. in length and 3.5 to 2 cm. in width, with a corresponding increase in the size of the overlying skin. The uterus was about normal size, upright, movable, and smooth. The left ovary and tube were normal. A tumor the size of a tennis ball occupied the site of the right ovary. It was semisolid, movable, and not tender. The cervix was normal. The internal os was normal. The uterine cavity was of normal length and the Fallopian tubes were patent.

A diagnosis was made of a masculinizing tumor of the right ovary.

She entered the hospital Jan. 24, 1944, and was operated upon on January 29.

The red blood count was 5,430,000, hemoglobin 17 Gm., leucocytes, 8,000. Wassermann reaction was negative. Urine was normal. The basal metabolism rate was minus 20. X-ray examination showed a definite shadow in the right lower quadrant. Photographs were taken of the genitals, the breasts, and the lower part of the face. A voice record was attempted, but was not successful.

At operation the pelvic findings were the same as found on examination, a tumor of the right ovary the size of a tennis ball, both tubes, left ovary, and uterus normal. No palpable pathologic changes were found in the upper abdomen. The right ovarian tumor was removed. The patient made a prompt recovery and left the hospital on Feb. 12, 1944.

\*Presented before the Chicago Gynecological Society, Nov. 16, 1945.



*Pathologic Report.*—

*Gross description:* The ovary was slightly larger than a golf ball and was oval in shape and firm in consistency. The surface was regular, except for small cysts which bulged slightly from the surface, mostly on one side. The surface was of a translucent gray color. A cut through the center of the ovary revealed the presence of a rounded, sharply demarcated tumor mass which occupied most of the ovary. The tumor mass was homogenous in appearance and of a light yellowish tan color. It was not encapsulated from the ovarian substance which formed a bordering zone about the tumor measuring from 2 to 8 mm. in thickness. The small cysts in this ovarian tissue contained clear fluid. The tumor bulged from the cut surface, and lobular division of the tumor was indicated by a granular appearance of the cut surface.

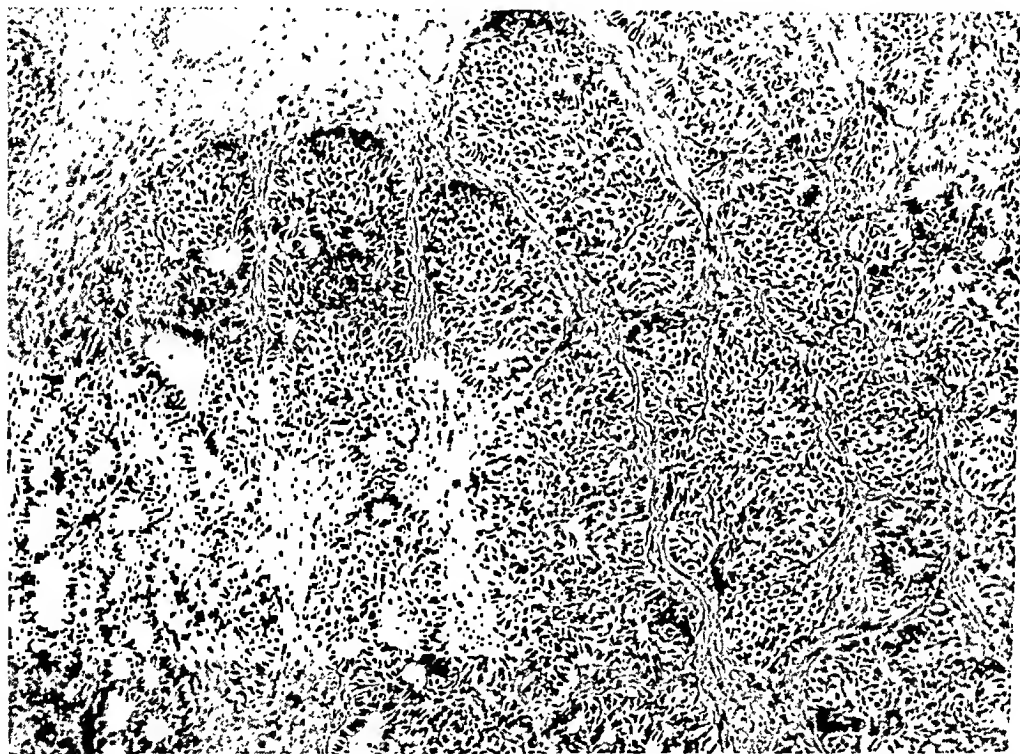


Fig. 2.—Moderately high power photomicrograph showing broad, radially arranged cords of epithelial cells composed of mixed acinar structures and more or less obscure tubules or solid masses of cells. Note practically complete absence of the interstitial type cells. Histologic diagnosis: Highly differentiated arrhenoblastoma of ovary (testicular adenoma of Pick).

*Microscopic description:* Rather broad irregular cordlike masses of deeply stained tumor cells were composed of both acinar or tubular structures and other groups of tumor cells which did not appear to have any particular arrangement. The cells did not vary much in size, and the shape varied from rounded to angular or slightly spindle shaped. The nuclei were nearly all central, and had a pyknotic appearance. The nuclei tended to assume the shape of the individual cells. In places the epithelial positions of the tumor narrowed down to cords which took a zigzag course through bordering zones of fairly dense fibrous stroma. The cells of these narrow cords were arranged at right angles to the direction of the cords. Lumens could not be demonstrated in the cords, but some of the cords appeared to end rather abruptly, in small acini. The stroma of the tumor was simple, and appeared to be quite dense, although the nuclei of the stroma cells maintained the oval shape typical of newly formed fibrous tissue.

of the epithelial cells, but one can say with fair certainty that definite alveolar or tubular arrangement was absent. It is remarkable that in a tumor showing so little differentiation in structure that interstitial cells should be so well developed.

*Diagnosis.*—Undifferentiated arrhenoblastoma of the ovary.

*Postoperative Course.*—On March 1, the patient had a normal menstrual period without pain, and on March 29, had a second normal period. There was a rapid change back to her feminine characteristics. When seen on June 17, there had been a weight loss of 24 pounds, the hair was falling from the face, arms, and legs, and her voice was much better. She was able to sing once more, and over the phone people no longer said "yes sir" to her. The clitoris was very much smaller and there was no dyspareunia. The red blood count was 4,120,000. The basal metabolism rate was plus 2.

She was seen again on Dec. 23, 1944, when she stated that her last menstrual period had occurred on October 23. Examination revealed a normal uterine pregnancy. The Aschheim-Zondek test was positive.

Under the care of Dr. William B. Serbin, she gave birth to a normal baby, weighing 7½ pounds, on Aug. 16, 1945, nineteen months after surgery.

At the present time (October, 1945) the breasts are normal, there is a free secretion of milk, and she is nursing the baby. She has none of the former masculine characteristics. The menstrual cycle is normal.

CASE 2.—Mrs. S. S., aged 20 years, dark complexion, married two years, no children, no pregnancies.

Menstruation began at twelve years, periods were regular, three to five days' duration, and very moderate in amount. There was no discomfort or pain. Menstruation ceased in February, 1943, and had not recurred up to the time of consultation on Dec. 6, 1944.

The main points in her history, in addition to the amenorrhea and sterility, were a rapid gain in weight from 118 to 170 pounds in eighteen months, largely an abdominal disposition of fat, and a rapid and increasing growth of hair on the face and body. She had to use a depilatory on the face every morning because the beard was so heavy. She had had intensive endocrine therapy for one year before consultation.

The general physical examination was normal, except for very large pendulous breasts and an exceedingly large, firm abdomen.

Pelvic examination showed the clitoris enlarged to three or four times normal size. The vulva, vagina, and cervix were normal. The left adnexa or fundus of the uterus could not be palpated. The right ovary was palpable and enlarged, but receded from the examining finger so that estimation of size was not possible.

The Wassermann reaction was negative. The red blood count was 5,510,000, the hemoglobin 16.5 Gm. (103 per cent). The urine was normal. The basal metabolism rate was minus 18. The Aschheim-Zondek test was negative. An x-ray examination of the abdomen gave no help in this case.

Surgery was advised because of the evidence at hand, and because of the great similarity of the laboratory findings to those in the first case. Operation was performed on Jan. 20, 1945. The uterus was about normal in size, shape, and consistency. The right and left tube and left ovary were normal. The right ovary was the size of a golf ball or small plum, of normal color and prolapsed. It was firmer than normal and slightly larger at the hilum. The ovary was removed. The patient made a good recovery and left the hospital January 28.

## ANOTHER CASE OF ARRHENOBLASTOMA\*

ARTHUR H. CURTIS, M.D., CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, Northwestern University Medical School, and Passavant Memorial Hospital)*

OVARIAN tumors arising from male directed cells tend to cause masculinization in previously normal women if the tumor contains cells which elaborate the male sex hormone; this has occurred in nearly one-half of the reported cases of arrhenoblastoma; in fact, symptoms of virilism are almost a prerequisite in the establishment of a diagnosis. Defeminizing phenomena, such as amenorrhea and decreased size of the breasts, occur in some cases.

Arrhenoblastoma is a rare tumor. Sixty-odd cases have been recorded in the literature.

Grossly, these tumors are often like granulosa-cell tumors but tend to be more nodular. They are almost always unilateral (mine was bilateral), are mostly solid, the cut surface frequently necrotic or hemorrhagic.

The various growths differ according to the stage in which development was arrested. The three arbitrarily distinguished types are (1) the highly differentiated testicular adenoma of Piek, (2) the undifferentiated, chiefly sarcoma-like, functionally most active growth, diagnosed by rudimentary tubules and sex-like cords of cells, (3) the intermediate group, of large size and presenting great variation in structure, occupying a midposition as to function. Our tumor belongs in the last-named group.

An arrhenoblastoma may be small, but it is usually readily palpable. The relatively benign character of the growth merits emphasis, even in those cases with a sarcomatoid structure.

### Case Report

I. C. (No. 3639), aged 52 years, the mother of two mature sons, and a widow for three years. The last menstruation occurred six months previously, and for the same period of time there had been hoarseness of the voice. Gradually increasing distress and fullness of the abdomen had been present for some months, but there was no pain until one week prior to consultation.

Marked hirsutism and deep huskiness of the voice were at once apparent. Hypertrophy of the clitoris and the enlarged abdomen suggested the probability of an arrhenoblastoma, even before bimanual examination. Abdominal and pelvic palpation revealed solid tumors, apparently of ovarian origin, which filled the pelvis and abdomen to above the level of the umbilicus. A uterus of essentially normal size was palpable, separate from the freely mobile tumors.

At operation, Oct. 12, 1943, both ovaries were found converted into solid tumor masses, each the size of a child's head. A plum-sized pedunculated myoma sat atop a well-placed uterus of normal size. Both tubes were normal. Palpation of the other abdominal viscera revealed one large stone in the gall bladder, a markedly indurated pancreas, and somewhat indurated kidneys. The entire uterus, both tubes and ovaries, and the appendix were removed.

\*Presented at a meeting of the Chicago Gynecological Society. Nov. 16, 1945.

The bands of stroma varied greatly in thickness from the wide bands which roughly divided the epithelial cords or masses, to narrow strands which tended to cross the epithelial cords dividing them into blocklike areas.

Interstitial cells could not be recognized in any of the sections. The ovarian tissue about the tumor mass contained primordial and developing follicles.

*Diagnosis.*—Highly differentiated arrhenoblastoma of ovary. Testicular adenoma of Pick.

*Postoperative Course.*—On February 1, there was a bloody discharge from the vagina for one day. On March 5 she had a regular menstrual period, flowing a good amount for five days. Periods have recurred regularly since that time. There has been a loss of 50 pounds in weight up to Sept. 10, 1945, without any special care or diet. There are large areas of alopecia on the face and body.

### Discussion

Both of these patients had similar signs. The undifferentiated tumor showed more effect on the external genitals than the differentiated growth, possibly due to its being five years older. The growth of hair was much more abundant and there was much more gain in weight, but with very little difference in the metabolic rate in Case 2. Both patients had high red blood counts, which is not consistent with the low metabolic rate and the large gain in weight. These, I think, are important signs in diagnosis of these growths, and particularly in young, healthy individuals. Bingle mentioned polycythemia in these cases but could offer no explanation for it. The response to surgical removal of the ovarian tumors was very prompt and very gratifying in both patients.

### Addendum

CASE 2.—May 8, 1946, a normal pregnancy of approximately thirty-two weeks' duration.

250 EAST SUPERIOR STREET

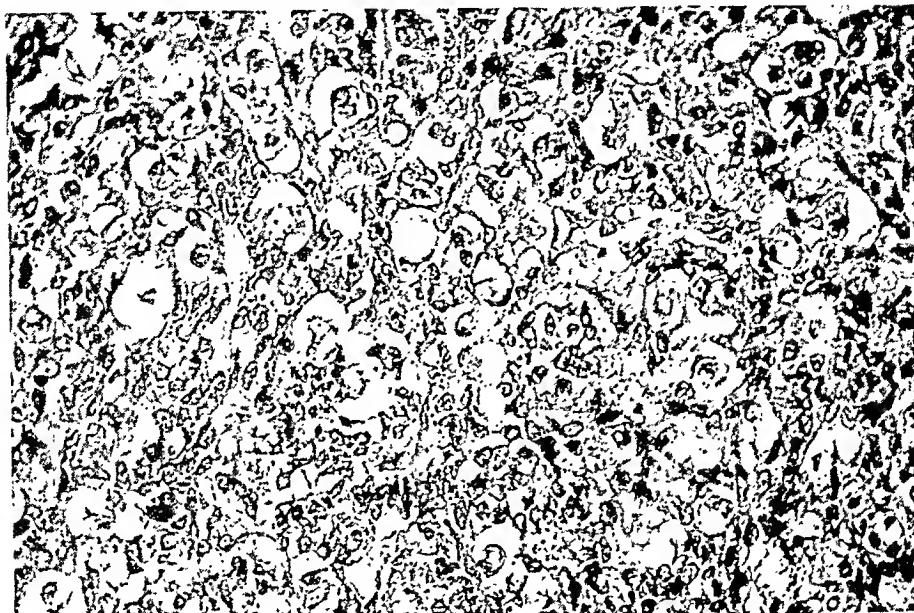


Fig. 3.—Arrhenoblastoma, case 3639. Diffuse sarcoma-like structure with slight tendency to tubule formation, characteristic of major portions of both tumors. (X200.)

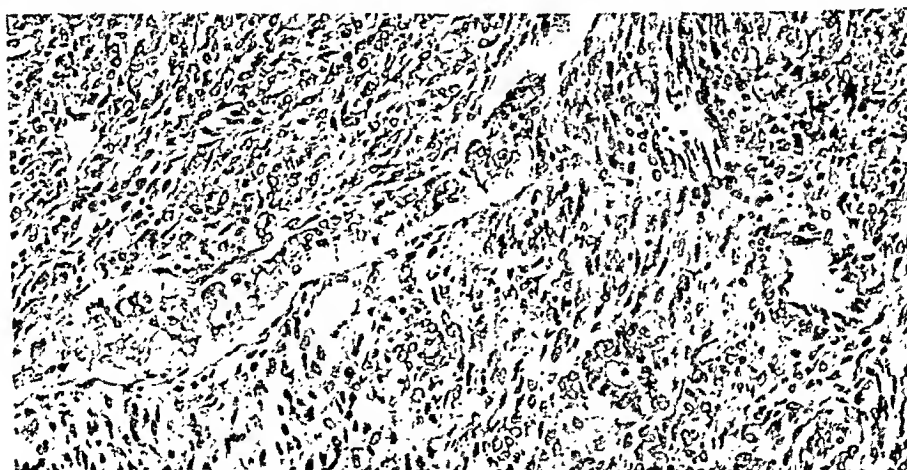
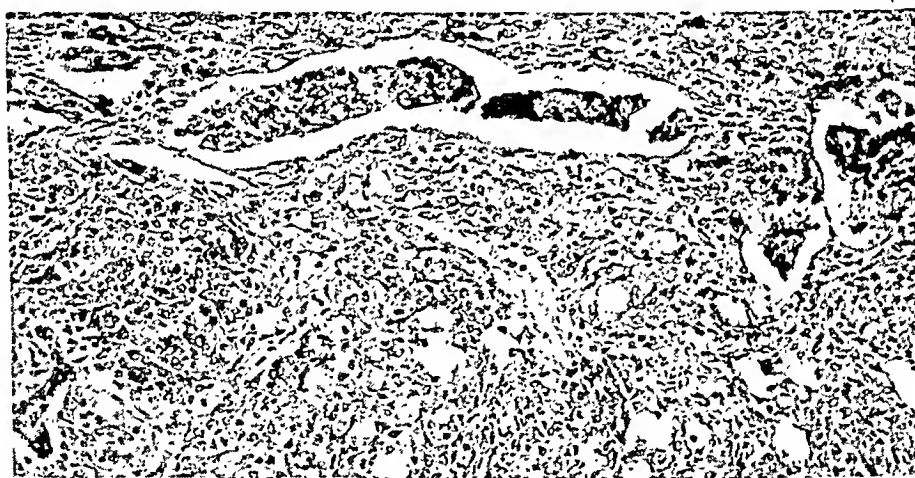


Fig. 4.—Arrhenoblastoma, case 3639. *Above.* Epithelial proliferation of solid strands, cords of cells and slight tubule formation, intermingled with a diffuse sarcoma-like growth. (X120.) *Below.* One solid strand and some minute cords and clusters of cells, also several atypical tubules, merging into a sarcoma-like and less malignant spindle-cell growth. (X132.)

Pathologic examination of the tumorous ovaries revealed two massive ovoid growths of almost identical size measuring 17 by 18 by 9 cm., and 17 by 13 by 10 cm. (Fig. 1).

The external surfaces of the two firm growths were markedly but smoothly nodular, with glazed milky tissue beneath the capsule in many areas, as from distended lymphatics. The color as a whole was bright red to dull cherry-red,

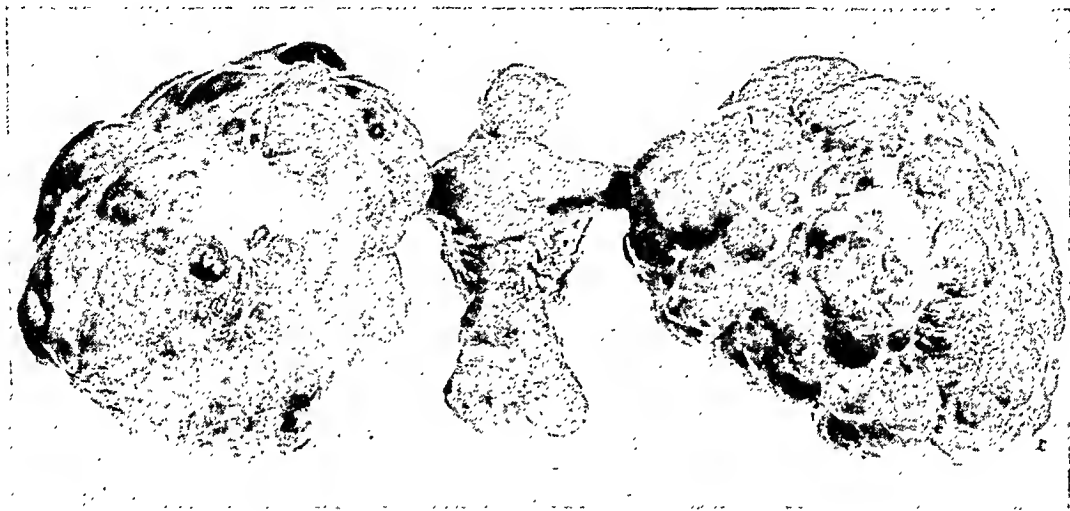


Fig. 1.—Arrhenoblastoma, case 3639. Photograph of uterus (myoma atop fundus) together with two ovarian tumors measuring 17 by 18 by 9 cm. and 17 by 13 by 10 cm.

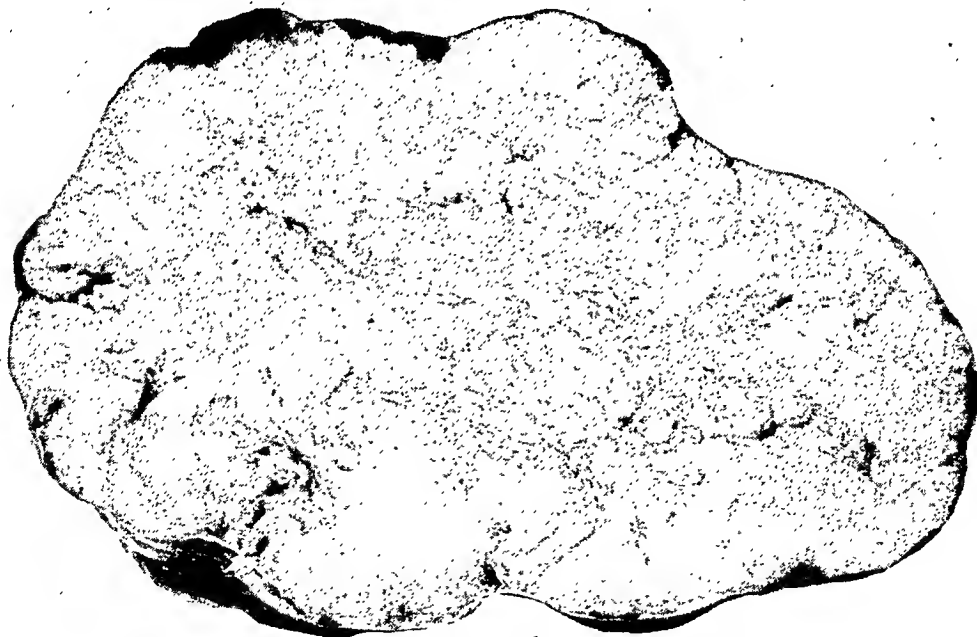


Fig. 2.—Case 3639. Cut surface of bisected arrhenoblastoma of ovary. 17 by 18 by 9 cm.

some areas gray-white. Nowhere was there surface ulceration, although there were many projecting minute nodules as well as large ones up to 5 cm. in diameter.

The cut surface of one bisected tumor (not illustrated) had many geographically irregular, extensive areas of gelatinous softening, in distinction from the one shown in Fig. 2, which was only slightly necrotic. The tumor

Registry and the work of this Committee has received favorable publicity in both the *Journal of the American Medical Association* and the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY. I look upon this Ovarian Tumor Registry as a potent source for important contributions to our knowledge of gynecologic pathology. This Registry is already rendering a fine service, and will permit our knowledge of ovarian tumors to expand with greater rapidity.

DR. VICTOR D. LESPINASSE.—I happened to read in a recent number of the *British Journal of Obstetrics and Gynecology* of a patient who had an arrhenoblastoma of the ovary becoming pregnant. When the baby was born it was a female, deformed in the same way that Dr. Greene's female rats were deformed when he injected testosterone into the mother. The deformity is a good deal like hypospadias in the male. It is interesting to see what an increased amount of testosterone will do in a pregnant woman. The patient reported in the *British Journal* did not have a very large clitoris. She had a good sized tumor and abundant facial and body hair.

DR. MARK T. GOLDSTINE.—Gynecologic pathology is a most interesting type of work and it requires that the clinician himself supervise and care for his own specimens.

As far as the outline of the tumor is concerned, I think this tumor is not of morphologic origin. I think the tumor originated in the ovary itself, and that it arose from the ovarian tissue.



tissue as a whole, although quite firm, was raw fish- or brain-like, gray-white, in some areas more vascular, almost telangiectatic. On the whole, the cut surfaces of the two tumors did not differ enough to merit separate descriptions.

The microscopic structure presented mostly a richly cellular alveolar configuration, the cells large and irregular, mostly oval (Fig. 3). This massive expanse of sarcoma-like tissue merged here and there with irregular tubules and cords of epithelial cells, some with a distinct lumen, others in solid strands, thus identifying the growth as an arrhenoblastoma belonging to the intermediate group (Fig. 4). The oft-repeated statement that gradation from the sarcoma-like cells directly traceable to epithelial cords demonstrates the epithelial origin of the tumor is open to question, for one finds also, as with thecoma cell tumors, a definite transition from the richly cellular growth to spindle-shaped stroma cells, richly cellular fibrotic tissue constituting a considerable portion of the tumor structure. It would appear, as with thecoma tumors, that it is immaterial whether the cells are sarcomatoid or definitely epithelial. Whether they arise from embryonal rests of mesenchymal origin, or from perverted growth of stromal elements, or owe their origin to one-sided development of a teratomatous tumor, is undetermined.

The massive size of the tumors is characteristic of the intermediate group of arrhenoblastoma. As stated, a bilateral growth is unusual.

The uterus was of generous size and contained two subserous myomas, the larger the size of a walnut. The opened uterus was of normal proportions except that the cervix constituted nearly one-half of the uterine length. In conformity with the usual tendency in this disease, the endometrium was more atrophic than normal in a patient only six months beyond her last menstruation.

The patient has had an uneventful clinical course since the time of operation. The voice has modulated, hypertrichosis has largely disappeared, and the clitoris has returned to normal size.

### Discussion

DR. GEORGE H. GARDNER.—Dr. Curtis' presentation of his adrenal-like tumor and his discussion of the accompanying problems, is an illuminating résumé of all that is now known about such tumors. Obviously, there are many features which are not yet well understood and which cannot be settled now with certainty. However, I am quite willing to accept the interstitial cells of the ovary as the origin of such adrenal-like tumors. On the other hand, I still am confused and a bit perturbed by the terms luteoma and luteinoma, and since world authorities doubt the existence of such tumors, probably the hypothetical luteoma and the nebulous luteinoma should be omitted both from the literature, and from our discussions. Although it is an acknowledgment of weakness, nevertheless it is a fact that, for the accurate identification of many unusual ovarian tumors, more is necessary than the mere histologic study of hematoxylin and eosin stained sections of these tumors. One must have additional information, namely, the clinical history of the patient and the benefit of special staining techniques to bring out distinctive features of tumor cells in order to arrive at a final diagnosis.

I wish to take this opportunity to bring to the Society's attention and to solicit your support for a project which was fostered by the American Gynecological Society in 1942. At that time an Ovarian Tumor Registry was established, and a Committee was appointed to study and classify ovarian tumors as they were submitted to this Registry. It was hoped thereby to accumulate a volume of material which would permit a better understanding of many ovarian tumors. The Chairman of this Committee is Dr. Emil Novak; consequently, at present, this Ovarian Tumor Registry is located in Baltimore. Among others the Committee includes Dr. Robert Meyer. Up to the present time only about 150 tumors have been submitted for survey, and I might add that very few have come from the Chicago area, even though the



### Summary

The total fluid removed during the fifty-six days and at the time of operation was 80,840 c.c., and weighed two hundred and twenty-three pounds. The difference of weight between the weight loss from the time of admission to the time of discharge and the weight of the fluid removed is due to the fact that there was a reaccumulation of fluid during this 56-day period. Unfortunately, the cyst wall was not weighed. However, it is safe to regard the combined weight of the cyst wall and fluid as in excess of 164 pounds.

This report is not primarily presented because of the size of the ovarian cyst, but in view of the interesting problem created because of the length of time that this patient's condition was undiagnosed, and the fact that she was treated for the conditions mentioned.

3254 NORTH 54TH STREET

## LARGE OVARIAN CYST

### Report of a Case

F. J. HOFMEISTER, M.D., MILWAUKEE, WIS.

*(From the Milwaukee Hospital)*

THE patient, Miss H. M., aged 58 years, was first seen in July, 1944, with a greatly distended abdomen. Her weight was 264½ pounds. The circumference of her abdomen was 62 inches.

This tremendously distended abdomen had been present thirty-four years, and had increased in size more rapidly in the last three years. She had been treated over this period of time by various reputable physicians for conditions varying from pulmonary tuberculosis with peritoneal tuberculosis, to decompensated heart disease. When first seen she was taking digitalis and using Salyrgan suppositories to reduce the "abdominal ascites."

Examination revealed the heart and lungs to be normal. The blood pressure was 122/75. The urinalysis and complete blood count was normal. A chest x-ray was normal. A gastrointestinal x-ray revealed the intestines displaced into the upper abdomen. The abdominal wall was so distended and so thin that the abdominal cavity could easily be transilluminated using a flash light. Large, distended, tortuous varicosities were present in the abdominal wall. The percussion note of the abdomen was dull. There was a distinct fluid wave. No shifting dullness could be elicited. There was little ankle edema, but varicose veins and small varicose ulcers were present on the extremities.

A diagnosis of probable ovarian cyst was made. Because of the tremendous distention, slow decompression to be followed by exploratory laparotomy was the treatment decided upon. This decompression was done by means of an indwelling, plain rubber catheter inserted through an ordinary trocar. Drainage was carried out over a period of fifty-six days in amounts varying from 1,000 c.c. to 1,500 c.c., depending upon the patient's condition. By the end of this 56-day period of time, 78,840 c.c. of fluid were removed. Six days after the final drainage, an exploratory laparotomy was done through a small midline laparotomy incision to first verify the presence of a cyst wall. This incision was then enlarged, dense adhesions to the abdominal walls and the abdominal viscera were freed, and a collapsed cyst was delivered. The origin of the cyst was in the left ovary. The remainder of the pelvis was left intact, 100,000 units of penicillin was instilled into the abdomen, and the abdomen was closed. The patient made an uneventful recovery, and was discharged from the hospital on the fifteenth postoperative day, weighing 100 pounds.

The thickened wall of the cyst was opened and was found to be unilocular, and contained an additional 2,000 c.c. of fluid. The fluid was green, opalescent, and serous in nature. The specific gravity was 1.028. The total protein was 7.15 grams. There were no tumor cells or bacteria found microscopically, and there was no growth on the culture plates. The microscopic sections of the tissue revealed a fibrous cyst wall containing few glandular elements. A diagnosis of benign, unilocular, serous cystadenoma was made.

The patient was last seen in February, 1945. She weighed 140 pounds and was living a normal life, after having been a semi-invalid for thirty-four years.

\*Presented at a meeting of the Chicago Gynecological Society, Nov. 16, 1945.

remarkable. A low classical incision was made in the midline. Four hundred cubic centimeters of blood clots were encountered and, because the head could not be delivered easily employing the hand as a vectis, the feet were grasped and a living infant extracted at 12:35 A.M. Aug. 21, 1945. It was estimated by subsequent measurement of clots that during a period of three minutes the blood loss totaled at least 3,000 cubic centimeters. During this time the placenta, which was partially separated anteriorly, was removed manually with some difficulty from its attachment on the right side. Intravenous pitocin was given as the baby was extracted, and five to ten minutes later the uterus contracted satisfactorily and the hemorrhage appeared to be controlled. The uterus was closed in layers and no bleeding or other abnormality was noted. Accessible clots and free blood were removed from the peritoneal cavity, although it was definitely felt that there was some free blood left in the upper abdomen. The abdominal wall was closed in layers with catgut and, because of haste, no stay sutures were employed. The skin was approximated with interrupted black silk sutures. The operation was accomplished in twenty-eight minutes.

Concurrently with the hemorrhage, profound shock rapidly developed. The radial pulse could not be palpated nor the blood pressure obtained. Respirations were shallow and accordingly the anesthesia was stopped and oxygen administered. Simultaneous infusions of whole blood and plasma were immediately started, and within forty minutes of the delivery of the baby 1,000 c.c. of blood and 500 c.c. of plasma had been administered under pressure. A temporary response occurred, but deep and prolonged shock again developed which had all of the signs and symptoms of the irreversible phase of this condition. During the first hour following operation 250 c.c. of clots were expressed from the vagina; thereafter the vaginal bleeding was somewhat excessive for a few hours, but because of a firm fundus at all times other than oxytocics, further investigation or therapy for this condition was not carried out. Replacement and supportive therapy were continued and by 9:00 A.M., eight and one-half hours after delivery, the patient had received 3,000 c.c. of whole blood, 2,000 c.c. of plasma, and 1,200 c.c. of saline as a vehicle, a volume equal to the total calculated blood volume at the time of operation, and for the first time she had definitely recovered from a state of shock. Supportive measures included oxygen by inhalation, external heat, vitamins K and C, adrenal cortical hormone, stimulants, digitalization, and tourniquets applied to the upper thighs. At noon the hematocrit was found to be twenty. There was no abnormal vaginal bleeding and no signs of intraabdominal hemorrhage, and the fundus remained well contracted. Because of the low cell volume an additional 500 c.c. of blood were given. One thousand cubic centimeters of 1/6 molar lactate was administered to combat the acidosis of shock and to minimize any possible kidney damage resulting from blood incompatibility. Additional blood was given three days later because the hematocrit was 21 and the hemoglobin 6.5 grams. There was no apparent satisfactory explanation for these disturbing low figures.

On the fifth day after the cesarean section, oozing of dark blood was noted from the upper portion of the incision. Further investigation immediately revealed a definite wound disruption. The abdomen was reopened and considerable old dark free fluid blood was aspirated; it seemed obvious that it had been there since the first operation. The uterus was pushed far over to the left side. The site of incision in the uterus appeared to be healing satisfactorily and the right broad ligament contained a hematoma completely filling the lower abdomen up to the level of the umbilicus. After evacuating the old free blood it was conclusively decided that there was no intraperitoneal bleeding whatsoever. The posterior layer of the broad ligament was opened. Exploration revealed a complete intraligamentary rupture of the uterus 9 cm. long. The

# AN UNUSUAL CASE OF RUPTURE OF THE UTERUS WITH MASSIVE HEMORRHAGE\*

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THE amount of bleeding associated with rupture of the uterus varies from minimal amounts on some occasions when the trauma occurs at the site of a previous operation to sudden and profuse hemorrhage in other cases which may be intra- or retroperitoneal. A recent composite statistical report by Morrison and Douglass<sup>1</sup> cites an average mortality of 50 per cent. Such reports, because of the infrequency of the complication, include patients with this accident that occurred one, two, or more decades ago. The inclusion of only the more recent cases would undoubtedly reveal a considerable decrease in this mortality figure. Our own experience during the past thirteen years in the New York Lying-In Hospital includes 19 instances of this accident in approximately 45,000 term and premature deliveries, an incidence of 1 to 2,388 cases, with a mortality of 3, or 15.8 per cent.

Rupture at the site of previous operation, at the time of version, following the administration of oxytocics, injudicious instrumentation, and spontaneous instances constitute the most common causes. Complete intraperitoneal rupture can most frequently be diagnosed, while the incomplete or complete retroperitoneal types may be unrecognized. Accidents similar to the case to be described have probably occurred; however, in a review of the recent literature I have not been able to find a report with circumstances quite comparable.

## Case Report

A 42-year-old white woman, gravida vii, para iv, was admitted for the sixth time on the evening of Aug. 20, 1945, at term, giving a history of moderate vaginal bleeding during the afternoon, followed by low back and abdominal pain.

The history is of interest. In 1938 at the age of 35 years, following a normal pregnancy, she was delivered of her first baby without difficulty by low forceps following a fifty-hour labor. The placenta was retained and, because of bleeding, it was removed manually; at which time it was found to be adherent to the posterior and superior wall and right cornu. Recovery following transfusion was uneventful.

The following year during labor she was found to have a face presentation (right mento transverse). It was impossible to manually rotate the head and accordingly delivery was accomplished by midforceps rotation and extraction. The baby weighed 4,000 grams. Two years later (1941) she was found to have a brow presentation which was converted to a face, and followed by spontaneous delivery. In both 1942 and 1943 uncomplicated spontaneous abortion occurred. In 1944 she was delivered of a stillborn infant at term in another hospital.

During the evening following admission only very slight vaginal staining was noted, but pronounced changes in the rate of the fetal heart tones were soon noted. In addition, the tonicity of the uterus increased. A diagnosis of partial premature separation of the placenta was made, and a decision to effect delivery as quickly as possible in the interests of the child by cesarean section was reached. Under nitrous oxide-oxygen anesthesia the abdomen was opened and the uterus found to be somewhat rotated to the right but not otherwise

\*Read at a meeting of the New York Obstetrical Society, Nov. 13, 1945.

a return to normal by the eighteenth day following the second operation, at which time the patient was discharged from the hospital completely recovered.

During the postoperative course the patient received approximately 2 million units of penicillin, 70 Gm. of sulfadiazine, supplementary vitamin therapy, and other supportive measures.

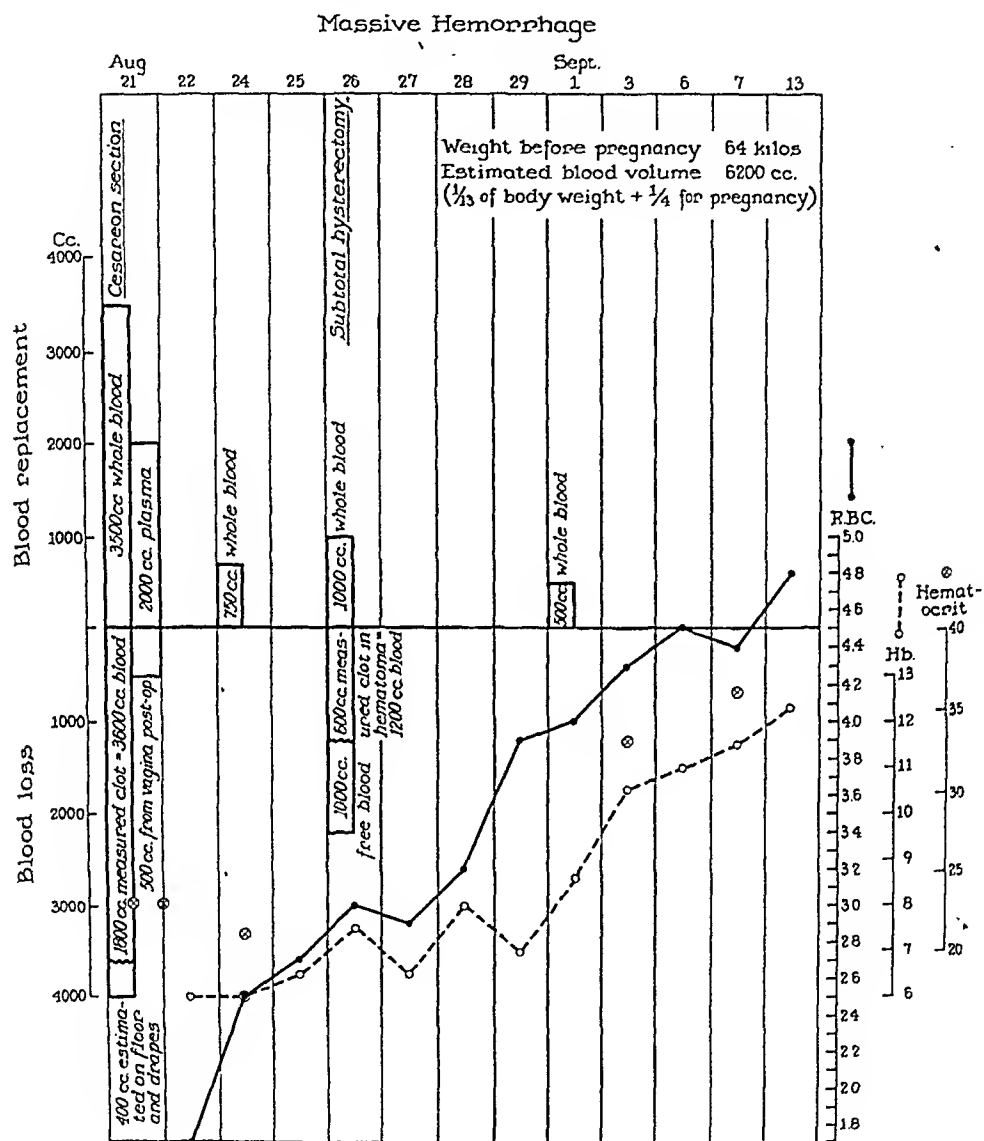


Fig. 3.

Pathologic examination of the uterus failed to reveal any possible cause for the rupture. The site of the cesarean section scar was only 4 cm. in length, with microscopic evidence of satisfactory healing. The uterine tissue in the region of the laceration showed some necrosis, hemorrhage, edema, and myometritis.

### Discussion

Data concerning the time and etiology of the rupture create the most interest. Several important questions might be asked, i.e.: Was the rupture spontaneous and probably incomplete and responsible for the initial symptoms requiring hospitalization? Did the patient have a partial premature separation of the placenta and did the rupture occur at the time of operation? Were there

relationships are illustrated in Fig. 1. Approximately 2,200 c.c. of blood was evacuated from the broad ligament and peritoneal cavity, and a hysterectomy was performed. The specimen is illustrated in Fig. 2. Satisfactory peritonealization was accomplished despite the friable edematous condition of the right broad ligament. A Miller-Abbott tube was inserted and the abdomen was closed in layers with catgut, reinforced with silver wire stay sutures. During the operation 1,000 c.c. of whole blood was administered.

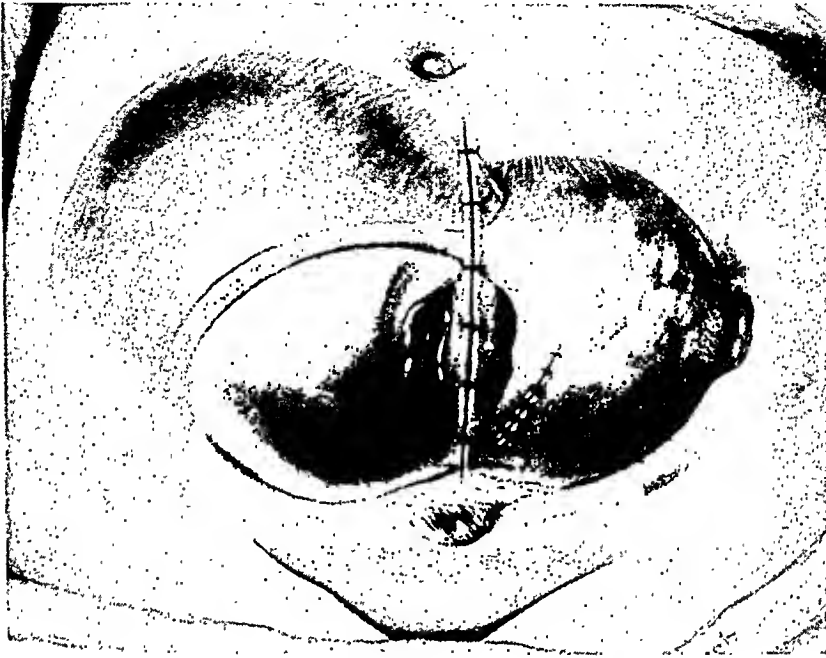


Fig. 1.

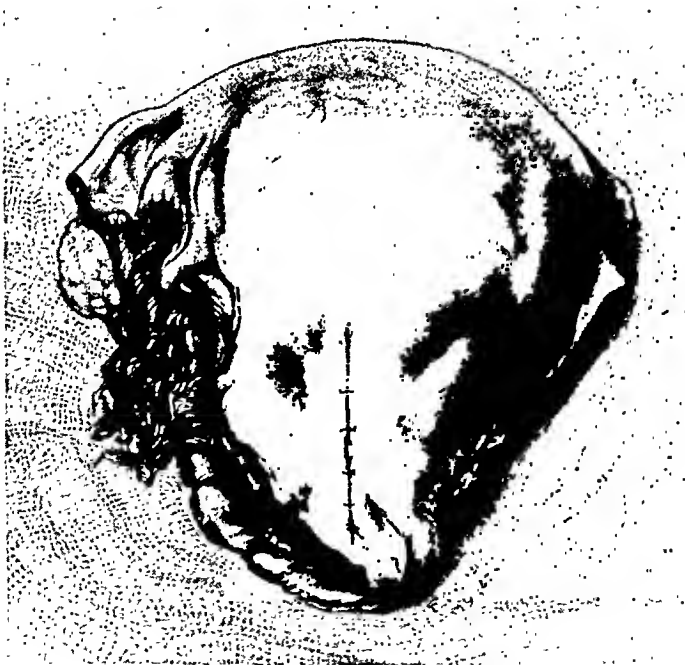


Fig. 2.

Figure 3 illustrates the blood loss and replacement and the hemoglobin, red blood count, and hematocrit levels. No essential change is noted during the period between the operations when bleeding presumably was occurring into the retroperitoneal space. A prompt rise in these curves thereafter is evident with

### Conclusions

1. The uterus can be ruptured during manual removal of the placenta at the time of cesarean section.
2. An infusion should be administered during cesarean section and blood available to add immediately in case of an emergency.
3. In the event of serious hemorrhage, multiple simultaneous transfusions administered under pressure, if necessary, provide a margin of safety not otherwise obtainable.

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### Discussion

DR. HOWARD C. TAYLOR, JR.—We have recently had a case of rupture of the uterus at Bellevue Hospital which raises some interesting points in connection with the physiology and pathology of hemorrhage after delivery.

This particular patient was delivered by midforceps early one morning and suffered a rupture of the uterus as a result. The rupture was not recognized for about three hours, when a mass appeared above the symphysis on the left side and gradually increased in size. As the patient appeared to be in only moderate shock and the operating rooms were fully occupied at the time, surgery was delayed for about an hour and a half more. Undoubtedly she bled a good deal during this time.

During the course of the hysterectomy which followed the blood pressure dropped so that for some minutes the pulse was imperceptible to the anesthetist. During this time the tissues took on a very dark color, and the uterine arteries at the time of their ligation were found impressively constricted.

This patient recovered, but she undoubtedly suffered severe permanent damage in several organs as a result of this period of lack of oxygen. She remained more or less comatose for about three days. During this time her urinary output dropped very low, and on the fifth day there was noted a considerable elevation of the nonprotein nitrogen of the blood. The patient also became permanently blind in one eye.

Renal function tests were undertaken about a week after the hemorrhage. The glomerular filtration rate and the renal blood flow were found to be only 50 per cent of normal. On a second examination about six weeks later these functions had returned to about 75 per cent of normal.

This patient apparently falls into a group in which severe hemorrhage and shock are associated with a temporary anoxia, formerly usually fatal, but now capable of successful therapy, as a result of prompt replacement of blood. In a few such cases, however, recovery will not be complete, because permanent damage will have occurred during the period of acute oxygen lack. The areas most susceptible appear to be in particular brain tissue, renal tissue, and perhaps the pituitary gland.

The case is perhaps important because it suggests that the effect of hemorrhage is not always limited to the acute episode. It is possible that in many other cases less easily recognizable, but perhaps significant, injury occurs.

The patient is presented as one who went through an episode somewhat similar to that reported by Dr. Douglas, but one in which the subsequent permanent injury was sustained.

anatomic changes in the uterus following the previous unusual obstetric history, and, if so, did such pathologic anatomy predispose to the present accident? From a consideration of the available facts which, of course, does not preclude other possibilities, it would appear that the most likely explanation is somewhat as follows: The initial symptoms were caused by a small area of separation of the placenta. Following hospitalization and during observation this area increased in size until signs of fetal asphyxia and increased tonicity of the uterus developed. The presence of clots in the uterus indicated a partial separation, but, of course, did not preclude the presence of an incomplete rupture. The initial hemorrhage was of such massive proportions that the placenta was removed manually with difficulty, and the blood prevented this being done under direct visionary control. It would, accordingly, appear that the patient had a partial premature separation of the placenta with a portion of the remainder unusually adherent. During the process of separation the muscle of the uterine wall was traumatized. The size of the rent may have increased post partum because of the hematoma that subsequently developed.

The hemorrhage occurred from large vessels in the incision and from the placental site. It was promptly controlled by the retraction of the uterus and the general circulatory collapse. The sense of some degree of security by having an infusion running and blood available in the operating room on such an unpredictable occasion can well be imagined. The prompt employment of large quantities of blood and plasma administered through multiple sites with a maximum gravity effect, and pressure if necessary, is absolutely essential in the management of such emergencies. The development of secondary shock and the subsequent failure of the hemoglobin, red blood cell count, and hematocrit to rise suggested additional blood loss. A second operation, or vaginal examination, however, did not appear indicated because of the absence of signs of intraperitoneal or vaginal hemorrhage, and the reasonable satisfactory condition of the patient until the wound disruption on the fifth postoperative day. The subsequent prompt and progressive rise of these blood factors followed a very satisfactory course.

The urgent necessity for blood in this patient developed within a matter of three minutes and, because of routine preparations, it was possible to start replacement almost immediately. Reliance upon a single intravenous apparatus which is subject to failure upon such occasions does not provide the patient with all means at hand to insure her recovery. Molar lactate solution should be administered through one of the infusion sets as soon as practical to render the urine alkaline which will minimize untoward effects on the kidneys in the event of blood incompatibility, which is always possible when many bloods from different sources are employed.

### Summary

A case report is presented of a patient operated upon for partial separation of the normally implanted placenta. Massive hemorrhage (3,000 c.c.) occurred within a matter of three minutes after opening the uterus. The placenta had to be removed manually, and it would appear that the uterus was unknowingly ruptured during this procedure. The initial measured blood loss was in excess of one-half the estimated blood volume, and simultaneous replacement of blood and plasma by multiple transfusions during the day of operation represented eight-ninths of the estimated blood volume. The calculated blood volume of the patient at the time of operation was 6,200 cubic centimeters. The total blood loss was estimated at 5,700 cubic centimeters and the replacement of blood and plasma amounted to 7,750 cubic centimeters.



*Clinical Course.*—Operation was performed on Aug. 23, 1943. Under ethylene-ether anesthesia a midline subumbilical incision was made through the skin and subcutaneous tissue. Enormous distention of the abdominal wall had already retracted the rectus muscles laterally. The peritoneal cavity was opened. The only structure visible was an enormous cyst wall, and it was estimated that the cyst weighed about 20 pounds. An aspirating trocar was inserted into the cyst wall and about three quarts of a clear and slightly straw-colored fluid was aspirated. A slight amount of free peritoneal fluid was also present. The cyst had developed from the left ovary, and the left ovary and tube were resected. This specimen consisted of the collapsed cyst wall, plus a hard firm piece of tissue. After the resection of the left tube and ovary, there was noted a similar cyst existing in the right ovary about the size of a large indoor ball. However, at the base of this cyst, there was felt a hard concrete-like mass. This cyst was similarly deflated with the aspirating trocar. The right tube and ovary were now resected without any difficulty. On sectioning the hard concrete-like mass, at the base of the ovary, it was thought that the structure was a fibroma of the ovary which was coexistent with a serous cystadenoma. The abdominal cavity was found to be free from any bleeding points. Continuous chromic No. 1 catgut was employed to close the peritoneum and transversalis fascia. Continuous chromic No. 1 catgut was employed for anterior rectus sheath, and plain 00 interrupted sutures for subcutaneous fat. A continuous interlocking medium dermal suture was employed for the skin. The patient left the operating table in excellent condition.

*Pathologic Examination.*—The sediment from the centrifuged specimen of fluid consisted of a small amount of material which would occupy the volume of a sphere of 1 mm. in diameter. This material was grayish-white in appearance. It disclosed foam cells, polymorphonuclear leucocytes, and cholesterol clefts.

*Gross Examination.*—The left ovary measured 26 by 19 by 10 centimeters. It contained a cyst 20 by 15 by 7 cm., which was filled with clear straw-colored fluid and which was lined by a smooth, grayish-white membrane. A papillary projection 0.2 cm. in height projected into the lumen of the cyst. In the ovarian tissue at one pole of the cyst was a mass which measured 3.5 by 3 by 0.4 centimeters. This tissue was firm and the cut surface showed grayish-white interlacing bundles of tissue. Several small cysts were present, ranging in size from 0.2 to 1.4 centimeters.

The right ovary measured 10 by 7 centimeters. It contained a cyst measuring 5 cm. in diameter lined by a smooth grayish-white membrane and filled with clear straw-colored fluid. In the ovarian tissue outside the cyst was a firm mass of tissue measuring 5 by 3 by 2 centimeters. The cut surface of this tissue was grayish-white and showed interlacing bundles of tissue.

A section of Fallopian tube 6 cm. in length showed no important changes except for an occluded fimbriated end.

*Microscopic Examination.*—The cyst from the left ovary was lined by a ciliated low columnar epithelium with small papillary projections into the lumen of the cyst. The cyst in the right ovary was lined by ciliated columnar epithelium. No papillations were present.

The solid tumors consisted of spindle-shaped cells with single nuclei. These cells were closely packed together except for an occasional area where a large amount of intercellular substance was present. The cells in some areas were arranged in parallel rows, whereas in others a mosaic pattern was produced. Mitotic figures were very rare, and blood vessels were not numerous. Frozen sections of these tumors stained with sudan III showed no fat.

The tumors occurring in this case, namely fibroma and serous cystadenoma, are not rare. The fibroma of the ovary may be considered an unusual but not

# BILATERAL CONCOMITANT FIBROMA AND SEROUS CYSTADENOMA OF THE OVARY

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NO SATISFACTORY basis for the classification of ovarian tumors has yet been established. Pfannenstiel, Goodall, Olshausen, von Franqué, Waldeyer, Geist, and many others have attempted a classification, and the many efforts expended are mute testimony that each is lacking. The case herein reported presents an unusual combination of ovarian tumors, a fibroma, and a serous cystadenoma in each ovary. A diligent search of the literature has revealed rare mention of such a combination, and since the knowledge of the histogenesis of ovarian tumors leaves much to be desired, it appears timely to report the following case.

## Case Report

Mrs. H. P., a 70-year-old married woman, was admitted to the service of Dr. Copland on Aug. 21, 1943, with a complaint of swelling of the abdomen.

*Present Illness.*—About ten months previous to admission the patient noted that her dresses were becoming too small in the waist, yet she was not becoming any larger elsewhere in her body. Her stomach continued to grow larger and larger and she thought that if she had not changed life years ago, she might be pregnant. There was no pain associated with the enlargement of the abdomen, which now appeared to be the size of a full-term pregnancy. There were no gastrointestinal symptoms or swelling of the feet or ankles. There had been some shortness of breath in the past three months, and the patient noticed that she was more comfortable on a back rest. No veins on the abdominal wall had become more prominent, nor had the patient developed any hemorrhoids.

There had been no serious illnesses or previous operations. She had been married fifty years, had had four children, no miscarriages. She had had arthritis with the last pregnancy, and the child was born with "sore eyes." Menopause occurred at 45 years of age. During menstrual life there was no dysmenorrhea, menorrhagia, or metrorrhagia. No vaginal bleeding had occurred since menopause. The family history was negative for diabetes, tuberculosis, malignancy, syphilis, or nervous disorders. No women in the family had had a similar swelling of the abdomen.

*Physical Examination.*—The patient's blood pressure was 170/90; temperature, 98.6° F.; respiratory rate, 22; pulse rate, 75. The patient was a well-nourished woman weighing 170 pounds, and about 5 feet 8 inches in height. She did not appear acutely ill or depressed. The relevant physical findings were: Abundant amount of grayish-white hair; some mild temporal artery sclerosis; glasses for myopia; mouth edentulous; wears upper and lower plates; chest, few coarse râles over right base. The heart was not enlarged. The abdomen was very much enlarged with rounded contour. Skin was tense. No varicosities of abdominal wall. Mass in right side of abdomen as large as a watermelon. Vaginal examination showed a senile vaginal atresia. Rectal examination essentially negative. Extremities, several varicosities of both legs but not severe; posterior, tibial, and dorsalis pedal vessels were easily palpable.

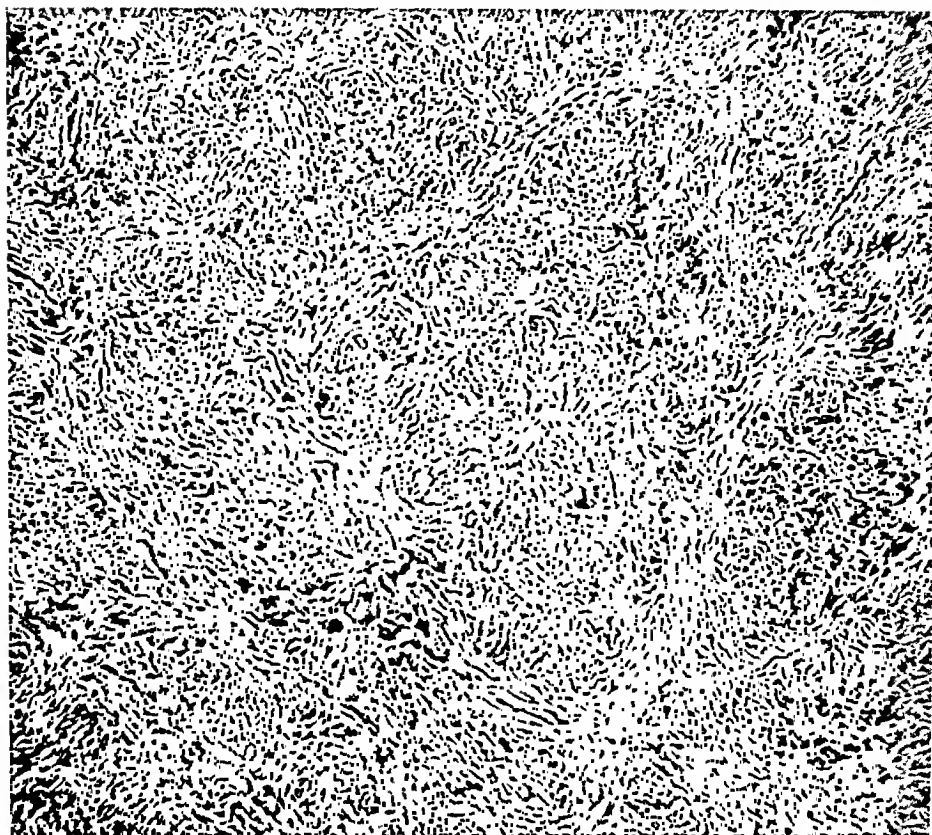


Fig. 3.—Mosaic pattern of spindle cells of fibroma from left ovary ( $\times 100$ ).



Fig. 4.—Spindle cells in parallel rows from fibroma of right ovary ( $\times 100$ ).

infrequent tumor and has been recognized as the most common connective tissue tumor of the ovary. Barzilai credits it with representing 1.7 per cent to 5 per cent of all ovarian tumors. However, benign solid tumors of the ovary are much less frequent than benign cystic neoplasm. Boyd states that serous cyst adenomas form  $33\frac{1}{3}$  per cent of cystic tumors of the ovary. Thus, this case pre-

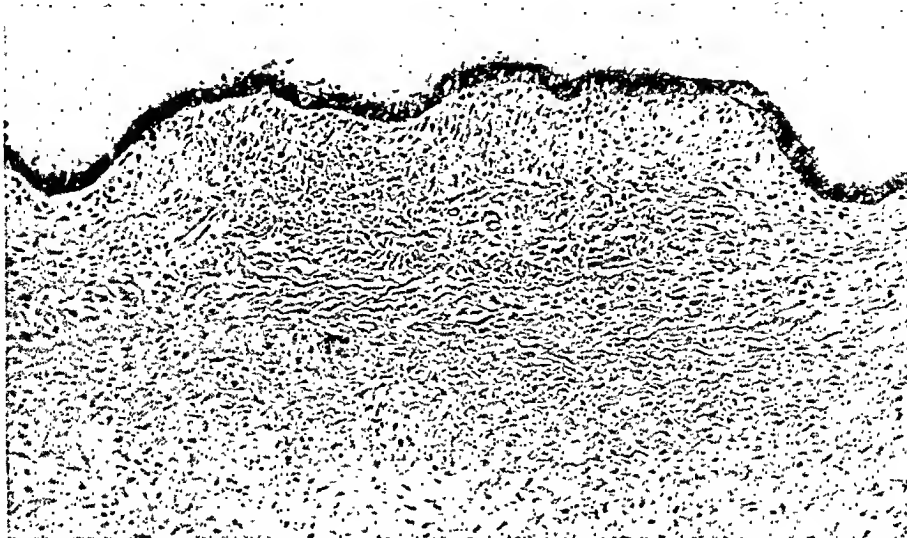


Fig. 1.—Ciliated columnar epithelial lining of cyst from right ovary (X100).

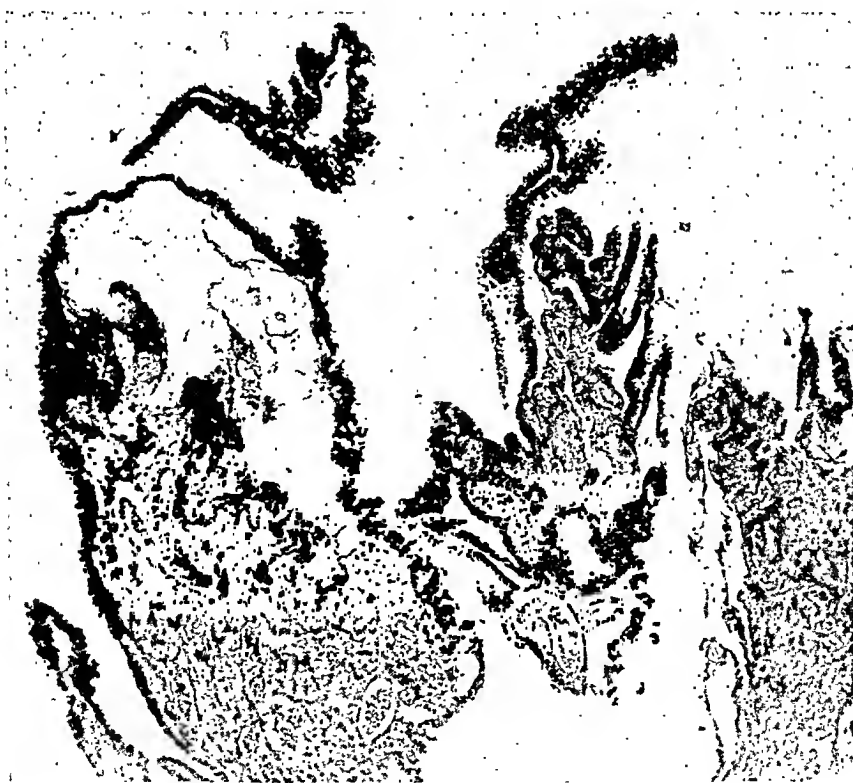


Fig. 2.—Papillation in cyst from left ovary (X80).

sents a combination of the most common benign solid ovarian tumor and the most common benign cystic tumor of the ovary, yet this combination is most unusual. The age of the patient, 70 years, is not of particular significance, for ovarian neoplasm can occur at any age. Downes found an ovarian tumor in a 7-month-old infant, and Spencer reported ten ovarian tumors in women over 80 years of age.

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The incidence of the coexistence of multiple ovarian tumors has given rise to a maze of conflicting and confusing statistical studies. The best explanation of this fact is Ewing's statement: "Statistical studies of multiple tumors have included in one category so many events of widely different significance that no general conclusions of any value can be drawn from them. The validity of assuming the existence of a general predisposition to cancer based on such statistical studies may be doubted."

This particular case represents an incidence of multi-centric growth of varying tumors in the same organ. It is possible that the term "multi-centric" is erroneous, but according to the present-day knowledge of the histogenesis of the ovarian fibroma and ovarian cystadenoma, such usage of the term multi-centric appears to be proper.

The fibroma of the ovary is considered to be of stromatogenous origin, but its definite histogenesis is not clear. Transitions from fibromas to adenofibromas have been described by Orthmann, Schottlaender, and others. Fibromas are often bilateral; as have been noted by Pfannenstiel, Kroemer, Geist, and others. Such was the instance in the present case: Figs. 3 and 4 show the typical dense bundles of spindle cells in mosaic and parallel arrangements; they do not show any evidence of mitoses or irregularity of the cells, so there is no difficulty in eliminating a malignant type of growth.

The bilateral papillary cystadenomas were unilocular, the left being unusually large, and the right being of usual size. The cyst from the left ovary was lined by a ciliated low columnar epithelium with small papillary projections into the lumen of the cyst. The cyst in the right ovary was lined by ciliated columnar epithelium, but no papillations were present. Although serous cystadenomas are frequently bilateral, they are not usually seen in a woman of 70 years. There was no evidence of malignant changes in either cyst. Geist states that papillary cystadenomas are frequently associated with other types of ovarian neoplasm, which may occur in the same ovary, but are more often in the opposite one. He states that associated fibromas have been reported.

There is no question that the serous cystadenoma originates from the germinal epithelium of the ovary. Novak states: "The chief evidence for this statement is that possible gradations can be demonstrated from simple invagination . . . to the fully formed papillary cystadenoma." The germinal epithelium varies greatly in its invasive qualities, as is demonstrated by the fibroadenoma of the ovary. However, this type of growth is not to be confused with the growth reported in this paper.

A cystadenoma, as well as a fibroma, may originate in a Brenner tumor. Meyer showed that the connective tissue response may assume huge proportions in some of these cases, so that tumors weighing several pounds may result. In the case under discussion there does not appear to be any resemblance to a Brenner tumor.

### Summary

1. A case of bilateral ovarian fibroma and serous cystadenoma is reported.
2. Although this combination of ovarian growths has been previously reported, according to Geist, the incidence is extremely rare.
3. This combination of growths represents the most frequent benign solid ovarian tumor and the most frequent benign cystic ovarian tumor.
4. Both growths assumed large proportions and occurred in an elderly female long after the menopause.
5. A similar combination of growths is sometimes associated with a Brenner tumor.

terior segment anthropoid and the anterior segment gynecoid. The ischial spines were prominent. Position of the fetus was right occiput transverse.

The patient developed a "running nose" on August 28. Examination showed a coryza with hyperemia of both tonsillar regions. Pain was present over the angle of the left jaw. A firm swelling occupied the pre- and infra-auricular area on the left, of about 3 by 5 centimeters. This had a definitely hard border outlining the area of the parotid gland. On this day labor was still described as poor, but the fetal heart was still good, being 128 beats per minute. Intravenous fluids were given continuously to supplement the oral intake which was small.

Consultants from the Contagion Service of this hospital diagnosed this complication as an acute left suppurative parotitis. A purulent, white discharge was expressed from the orifice of the left Stenson's duct, and a pouting of the orifice was seen.

X-ray of the jaw at this time revealed no calcified shadows in the region of the left Stenson's duct, or in the left parotid region. The temperature on August 28 was never above normal. On this day, a white blood count in the forenoon revealed 7,640 cells with 68 per cent polymorphonuclear leucocytes, 12 per cent transitional cells, and 20 per cent lymphocytes. A repeated blood count that evening revealed 9,500 white cells, with 84 per cent polymorphonuclear leucocytes, and 16 per cent lymphocytes. A catheterized urine specimen on the preceding day (August 27) was negative.

On the recommendation of the consultants, the patient was started on 2 Gm. of sulfadiazine at once, and 1 Gm. every four hours thereafter, with double the amount of soda bicarbonate for each dose. Irrigations of the mouth with a normal saline solution, and warm applications to the outside of the left jaw were also used. The sulfadiazine was continued for about forty-eight hours.

An attempt was made on August 28 to stimulate uterine contractions, which were described as poor in quality. A soapsuds enema, immediately followed by 60 c.c. of castor oil was given, and in one hour the soapsuds enema was repeated. Six grains of quinine hydrochloride were also given. Since the patient made little more progress, in the evening she was also given  $\frac{1}{4}$  grain of morphine sulphate which gave her about five hours of sleep. After she awoke, the pains were very strong. One and three-fourths hours of such pains brought her up to full dilatation. With a low forceps, an 8-pound male infant was delivered after eighty-seven and one-half hours of labor.

On the day of delivery, August 29, her temperature was 101.0° F., and the parotitis was unchanged. The mass on the jaw began to decrease in size within about twenty-four hours after delivery. Blood count done on August 31 showed that her white blood count was 10,000, with 70 per cent polymorphonuclear leucocytes, 5 per cent transitional forms, and 15 per cent lymphocytes. On the first day post partum, her temperature was 99.8° F. Mother and baby were discharged on the ninth day post partum in good condition. No vestige of the parotitis was present on discharge.

### Comment

The relationship of the parotid gland to systemic disorders has never been satisfactorily explained. It has long been known that parotitis occasionally occurs as a grave complication in infectious fevers. Paget<sup>6</sup> in 1886 pointed out that parotid bubo might appear secondarily, as a rare complication following operations and injuries to pelvic and abdominal organs. About 101 cases were collected by him from both the literature and his experience. Parotitis of all kinds following septic abortion and puerperal infection, on the other hand, has been described by several observers.<sup>6, 8</sup>



## ACUTE SUPPURATIVE PAROTITIS COMPLICATING PREGNANCY AT TERM

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PAROTITIS as a complication of pregnancy is infrequent, and the acute suppurative variety is very rarely described in the literature. In approximately the last forty-five years, both the *Quarterly Cumulative Index to Current Medical Literature* and the *Index Medicus* have listed only three articles<sup>3, 6, 8</sup> dealing with this complication in pregnancy. Two of these are in foreign journals,<sup>3, 8</sup> and the third is a parotitis following an induced abortion.<sup>6</sup> One of the two articles published abroad<sup>8</sup> deals with a heterogenous collection of different forms of parotitis (i.e., epidemic, suppurative, and parotitis relative to carious teeth) in eight cases of pregnancy.

Since this complication is described so infrequently in the literature in relation to pregnancy, we are reporting the case of M. B., who was delivered on the Obstetrical Service of Queens General Hospital on Aug. 29, 1945. In a survey of the statistics of this institution, we find that from Nov. 1, 1935, to Nov. 1, 1945, there were 14,517 deliveries. There was one other case of acute parotitis complicating pregnancy reported in this interval, and this latter case, on review, is apparently the epidemic variety of parotitis. So that, over a period of ten years in this institution, there was only one case of acute suppurative parotitis in pregnancy. It has been stressed that the prognosis is grave. The following is a report of a complete and uneventful recovery in such a case.

M. B. (A-79520), a 27-year-old, white, married, primigravida, a housewife, was admitted Aug. 26, 1945. Past history was irrelevant, except that she had mumps three years before admission. Antepartum course was essentially uncomplicated. Last menstrual period was Nov. 15, 1944; expected date of confinement, Aug. 22, 1945. The blood Wassermann done in the antepartum clinic on May 31, 1945, was negative. Labor pains had begun at 6:00 P.M. on Aug. 25. On admission, "pains" were coming about every fifteen minutes. Bag of waters was intact.

Examination on admission revealed a moderately well-developed and well-nourished, white woman weighing about 120 pounds and in no distress.

The tonsillar fossae were both slightly injected. The nostrils were negative. Facies was normal and symmetrical. Blood pressure was 135/80. The fundus was 2½ cm. below the xiphoid process. Fetus was estimated to be about 7 pounds. Position of fetus was believed to be right occipitoposterior. Fetal heart was 148 beats per minute in the right lower quadrant.

On rectal examination, the cervix was 2 cm. dilated and thick. The head was three fingers above the spines.

The temperature was normal. Urinalysis on August 26 was negative. Hemoglobin at this time was ten grams. Kline test on August 29 was negative. Patient was blood type O and Rh positive.

The uterine contractions were of desultory type on August 26. On August 27, the contractions were recorded as occurring every five minutes, but the head was still unengaged. After forty-three hours of such progress, x-ray pelvimetry was done, and showed a moderate-sized asymmetrical pelvic inlet with the pos-



## ENTEROUTERINE FISTULA

### With a Review of the Literature and Report of an Unusual Case<sup>1</sup>

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THE reported occurrence of fistulous openings between the bowel and the uterus is very uncommon. In 1933 Danforth and Case collected 58 cases appearing in the literature for the past two hundred years. Since then an additional 20 cases have been reported. All of these 20 do not appear with full information, so that complete statistical summarization is not possible. Some are only mentioned in articles and are apparently cited from personal communications, or they are referred to in the discussion of the paper. Terechoff, in reporting a case, mentions seven additional cases which he knew to exist without including the full data on them.

*Method of Production.*—Le Jemtel in 1909 predicated three causes. The first is either traumatic or spontaneous rupture of the gravid uterus with a loop of intestine entering the tear; the bowel is pinched with subsequent necrosis and fistula formation. Peritonitis with abscess formation is a second cause, when the abscess ruptures into the bowel and the uterus simultaneously. The third cause, carcinoma, usually of the body of the uterus, occurs when the malignant tissue undergoes ulceration and necrosis with the development of a fistula between it and any loop of large or small bowel which becomes adherent. More recent reports mention a fourth cause: as the result of faulty technique during uterine curettement. The fistula results from the puncture of the uterine wall with concomitant injury of the bowel. Of the total cases, 42 followed obstetric injuries, 16 were the result of inflammatory processes, 9 were caused by carcinoma, and 11 followed uterine curettement.

Some fistulas developed from unusual pathology. Dwyer reported a woman with spontaneous rupture of the uterus at six months' gestation with a fistula between it and the small intestine due to pressure of the fetal cranial bones. The fetus was finally extracted thirteen months after the onset of pregnancy. Schmid reported a fistula between the uterus and the large and small intestine caused by sigmoidal cancer. This was the only instance of the nine mentioned in which the carcinoma did not originate in the body of the uterus. Naremov, as quoted by Terechoff, treated a case caused by ulcerative colitis of the large bowel.

*Location of the Fistula.*—In many of the reports the location of the bowel opening was not mentioned, while in some the exact site of the communication could not be determined. Of those allowing analysis, in eighteen the fistulous tract was between the small intestine and the uterus, and in seventeen between the large bowel and the uterus. In three instances both large and small bowel had communications with the uterus. Neugebauer reported two cases of fistula between the stomach and the uterus.

*Treatment.*—Crossen and Crossen state: "intestinouterine fistula is so rare that generalization is not possible." They feel that whether the fistulous tract is connected with the uterus, vagina, or bladder, it is best handled by abdominal section with mobilization and separate closure of the bowel wall. They also believe that in cases of small fecal leakage plenty of time should be given for scar tissue contraction to close the fistula spontaneously before subjecting the patient to the hazards of operation.

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It appears, from the reports of cases of postsurgical and obstetric parotitis, that the etiology of acute suppurative parotitis might be found in two sources,<sup>6</sup> local or general. The first source of infection probably enters the gland via Stenson's duct. From a review of other cases of parotid gland involvement, it is apparent that the oral cavity has a very important part in the formation of parotid bubo. A large number of different organisms are known to inhabit the mouth, and under normal circumstances they are harmless. The patient's local resistance may be lowered, or the oral tissues may be traumatized, as from too vigorous swabbing of the mouth, or by the drying effect of an anesthetic, or by blood loss, or the depletion of body water, either from limited fluid intake or vomiting. Under such circumstances, otherwise innocuous bacteria might be conceived as invading the parotid through the duct of Stenson. There might also be a direct extension of infection from any area adjacent to the gland, as the ears or teeth.

The second source is believed to be a metastatic process, in which bacteria are conveyed to the parotid from another more distantly located organ, by the blood or lymph. Anatomically considering this explanation, it is to be noted that the parotid is the only one of the three salivary glands which contains lymph nodes. A slowing of the blood or lymphatic streams at the parotid, especially if the resistance of the patient is lowered by a debilitating condition, may produce a sufficient number of organisms to overcome the resistance of this tissue.

The most commonly found offending organism in acute suppurative parotitis is *Staphylococcus aureus hemolyticus*. This organism is one of the inhabitants of the nasopharynx. *Streptococcus viridans* is the second most important cause, but in contrast to the *Staph. aureus*, which causes the acute parotitis, the *Strep. viridans* produces the recurrent form of parotitis. *Pneumococci*, the third most commonly found organism, may cause either type of disease. *Odium albicans* and *Bacillus coli* are some of the bacteria which are less frequently found.

**Treatment.**—Prophylactic therapy is the best. Good hygiene, especially oral hygiene, and more attention to the fluid intake of the patients should be carefully observed. In those cases where no fluctuation has taken place, conservative therapy is used. This consists of hot boric acid applications, irradiation, irrigations of the mouth, and sulfonamides. It is felt that <sup>2, 4, 5, 7, 9</sup> in severe cases, incision and drainage should be done as early as possible. It is not wise to wait until frank fluctuation occurs before doing an incision and drainage, as necrosis and gangrene may appear before the fluctuation can be noted through the dense parotid fascia.<sup>9</sup>

Indebtedness for assistance is due to Dr. E. A. Fleming, Dr. Alexander Gross, and Dr. Arthur A. Goldfarb.

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to a mass which involved the rectosigmoid. As would be expected, there was no further discharge through the cervix or from the rectum, but the abscess drainage wound continued to drain fecal pus in small amounts intermittently. The patient was ambulatory. She gained fifteen pounds in weight.

Laparotomy was then performed to repair the fistulous tract. On exploration the uterus was found drawn to the left and adherent to the left adnexal mass. The only structures easily recognizable were a piece of omentum and a loop of ileum three feet from the ileocecal valve which was adherent. Continuing into what was the sigmoid colon. The extent and size of the other pelvic organs could not be immediately determined. The mass which measured about 10 cm. in diameter was attached to the abdominal wall in the area of the previous drainage. The omentum and the small bowel, which was adherent in two places forming a U-shaped loop, were separated. Thickening of the proximal ileum indicated the presence of chronic partial intestinal obstruction. After separation of the ileum several small areas of denuded serosa were inverted. The right tube and ovary which were thickened and chronically inflamed could next be identified deep in the pelvis. The body of the uterus was separated from the mass. The sigmoid colon proximal and distal to the area of involvement was identified. In dissecting the sigmoid free, the fistulous opening between it and the adnexal mass was found. At this point the diameter of the sigmoid was constricted to a caliber of one-eighth normal size. Final separation of the tubo-ovarian mass from all surrounding structures was accomplished by freeing it from the anterior abdominal wall. It was removed after cutting the tube at its uterine attachment and ligating the infundibulopelvic ligament. The left broad ligament and the drainage hole in the abdominal wall were peritonealized. The cicatrized portion of the sigmoid colon was excised and an end-to-end anastomosis performed.

At operation it was impossible to be sure whether the sigmoidouterine fistula occurred because of inflammation arising in the left tube or ovary, or because of some inflammatory reaction originating in the sigmoid. The sigmoid was so involved in the infectious mass that its lumen had been almost completely obliterated where it was adherent. No diverticuli were seen in the rest of the descending colon and none was reported in the specimen submitted to the laboratory. Pathologic report of tissue removed showed chronic suppurative salpingitis and abscess formation of the left ovary. Section of the specimen revealed the appearance of ovary with scattered and numerous infected cysts. Microscopic sections of the largest cyst showed a scant amount of florid purulent content. The thick lining consisted of granulation tissue densely infiltrated with lymphocytes, polymorphonuclear leucocytes, and plasma cells.

The patient made an uneventful recovery. The area from which the tubo-ovarian mass had been removed drained purulent material for about ten days through the old left lower quadrant drainage wound. A barium enema three weeks post operative showed colonic continuity well re-established, with only slight narrowing of the bowel lumen. The spur of the transverse colostomy was therefore crushed with a Devine colostomy clamp. The bowel mucosa was subsequently dissected free from the skin and inverted to allow closure of the skin.

### Comment

Repeated attempts by different medical officers were made to obtain a history of instrumentation, but to no avail. The etiology was important not only from pathologic interest, but also in determining procedures to be instituted in producing a cure. It is believed that this patient had a chronic salpingitis with a cystic ovary on the left side. The ovarian cyst became inflamed with the

Graves, in his textbook, states that complicated fistulous tracts between the viscera are sometimes created through the medium of pus tubes or infected ovarian cysts. No instances, however, of a communication produced in this manner were found. The following case history is an example of a fistula resulting from this cause.

### Case Report

A 22-year-old white woman, a member of the WASP, became ill in November, 1944, experiencing severe abdominal pains, especially in the left lower quadrant. They were accompanied by moderate fever and malaise. Several weeks later, while at home on leave, she consulted a local physician who stated that she had a pelvic mass on the left side which should be operated upon. She did not accept his advice but returned to her duty station. A few days later she began to pass feces through the vagina. Since this occurred she had had no bowel movements through the rectum. She felt feverish, with the pain in the lower abdomen continuing. The menstrual periods had been regular; the last period occurred on November 15. She did not believe she was pregnant; she denied all suggestions of instrumentation.

Past history revealed an uncomplicated appendectomy in 1938. She had been married four years, and had had one child in 1941. The delivery was normal; no instruments were used. There had been no other pregnancies. For the past six or eight months she had noticed mild intermittent pain in the lower abdomen. The pain came in brief attacks, lasting several hours, especially after exercise. She also complained of mild chronic constipation.

On reporting to the hospital, a diagnosis of enterouterine fistula was made, and she was transferred to this hospital. Physical examination showed that she was acutely ill with marked dehydration and a high fever. With a speculum in the vagina a hemopurulent discharge was seen exuding from the cervix. A mass was felt in the left fornix contiguous with the uterus. The presence of a fistulous tract between the bowel and the uterus was proved by instilling water into the rectum and observing it as it returned through the cervix. The communication was thought to be high, inasmuch as four to six ounces of water had to be instilled in the rectum before any return flow occurred. No barium or other radiopaque substance was injected to delineate the tract because the patient was acutely ill. For several days whole blood, intravenous fluids, and nutritional supplements were administered; the mass was then drained through a left lower quadrant muscle-splitting incision. Four to five ounces of foul pus were obtained, which was found to be *Streptococcus viridans* of the coliaerogenes group.

Postoperatively the patient had several attacks of nausea with recurrent vomiting and abdominal distention necessitating tube suction drainage. Her temperature remained fairly normal, with several intermittent spiking elevations. Bowel movements through the rectum were resumed two weeks after drainage of the abscess. There was not complete drainage of the abscess, however, as evidenced by occasional temperature elevations and palpable enlargement of the left-sided mass. The incision was explored several times under pentothal anesthesia to re-establish drainage.

Therapy for the next several months consisted of frequent transfusions, vitamin supplements, and a high calorie diet. During this time the patient improved tremendously. Fecal drainage from the cervix continued, as well as passage of stools from the rectum. Because the fistula did not heal spontaneously, a Devine transverse colostomy was performed. Another reason was to defunctionalize the bowel prior to repair of the existing fistula. Exploration during this operation revealed that no exact delineation of the pelvic organs could be determined, except that the uterus was pulled to the left and adherent

## ABDOMINAL WALL FIBROMA (URACHAL?) SIMULATING OVARIAN CYSTOMA

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THE case described below is of interest from at least two aspects: (1) the confusion in preoperative diagnosis, and (2) the comparative rarity of the neoplasm in question. While there would seem to be no doubt that the removed tumor was a degenerating fibroma, we cannot, of course, be certain of its urachal origin because the mass had grown to a size which seriously distorted the normal anatomy of its site. Fibromas and fibromyomas of this region have been reported as urachal tumors by Begg (1931), and the normal anatomy of the urachus and its associated fasciae has been described recently by Hammond, Yglesias, and Davis. An extensive survey of neoplasms of the anterior abdominal wall by Pack and Ehrlich in 1944 (Memorial Hospital, New York) indicated that 55 per cent of tumefactions of all kinds in that area were benign tumors, and that 9 per cent of the latter were fibromas. No mention is made, however, of the possible urachal origin of any of the fibromas.

### Case Report

A. N., Hospital No. 4176, a 50-year-old white woman, was admitted on Feb. 15, 1945, with complaints of lower abdominal pain and vaginal bleeding. The last menstrual bleeding had begun on July 3, 1944. Having had fifteen previous pregnancies, the patient assumed in August that she was again pregnant. In October she believed she felt fetal movements, and these continued up to the time of hospitalization. In November she experienced five days of intermittent vaginal bleeding and was treated by a private physician for "threatened abortion." The same physician followed her as a prenatal patient until the onset of bleeding on the day of admission, and then referred her to the hospital with a presumptive diagnosis of "placenta previa." The vaginal bleeding was not excessive, but it was accompanied by cramplike abdominal pains at intervals of twenty minutes, and these the patient interpreted as "labor."

Physical examination revealed a 98-pound woman with blood pressure of 160/104, systolic murmur at the apex of the heart, moderate generalized distention of the abdomen, and a tympanitic percussion note over the upper half. No fetal heart sounds were audible. Extending 12 cm. above the symphysis pubis was a semisolid, somewhat mobile mass which seemed to contract when palpated. There was a small amount of old blood in the vagina and there was further blood exuding from the external cervical os. The cervix was hypertrophied and exhibited cervicitis and erosion. Anterior and superior to the cervix there was a mobile cystic mass, estimated to be 14 cm. in diameter, and a uterus of normal size lay posterior to the cystic mass. A probe was inserted into the uterine cavity to a depth of 3 inches. The adnexal areas and rectum were normal to palpation. The immediate diagnostic impression was: pedunculated ovarian cystoma, no evidence of pregnancy.

Further study showed normal urine, hemoglobin 12 Gm. per 100 c.c., leucocyte count 9,500 per cu. mm., normal thoracic roentgenogram, and normal

formation of an abscess which ruptured into the cavity of the uterus and into the bowel. The point of rupture into the cavity of the uterus must have been through the lumen of the tube, inasmuch as no other communication with the body of the uterus could be demonstrated.

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day of menstruation; there were cystic follicles in the ovaries, and the cervix showed chronic cervicitis with erosion.

*Conclusion.*—Degenerating fibroma of the anterior abdominal wall, essentially normal uterus (menstruating), and multiple ovarian follicular cysts.

### Summary

A lower abdominal mass in a 50-year-old woman, para xv, was first mistaken for a pregnant uterus, later assumed to be an ovarian cystoma, and finally at operation demonstrated to be a degenerating fibroma of the anterior abdominal wall.

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cystogram. X-ray examination of the abdomen showed no evidence of pregnancy nor any calcification within the tumor mass.

On the third hospital day exploratory laparotomy, under spinal anesthesia, revealed an extraperitoneal tumor lying just anterior to the parietal peritoneum and immediately superior to the apex of the urinary bladder. The irregular semi-solid mass measured 15 by 14 by 12 cm. and was quite easily shelled out intact, although it had a fibrous pedicle superiorly which ran toward the umbilicus, but gradually lost its identity in the surrounding connective tissue (see Fig. 1). There was no direct connection between the surface of the tumor and the wall of the bladder. Because of the patient's age and the uncertainty as to the cause of her uterine bleeding, total hysterectomy and bilateral salpingo-oophorectomy were performed prior to closing the abdominal wall. The subsequent course was uneventful and the patient left the hospital on the eleventh postoperative day. She was examined eight months after the operation and there was no evidence of recurrence of the tumor.

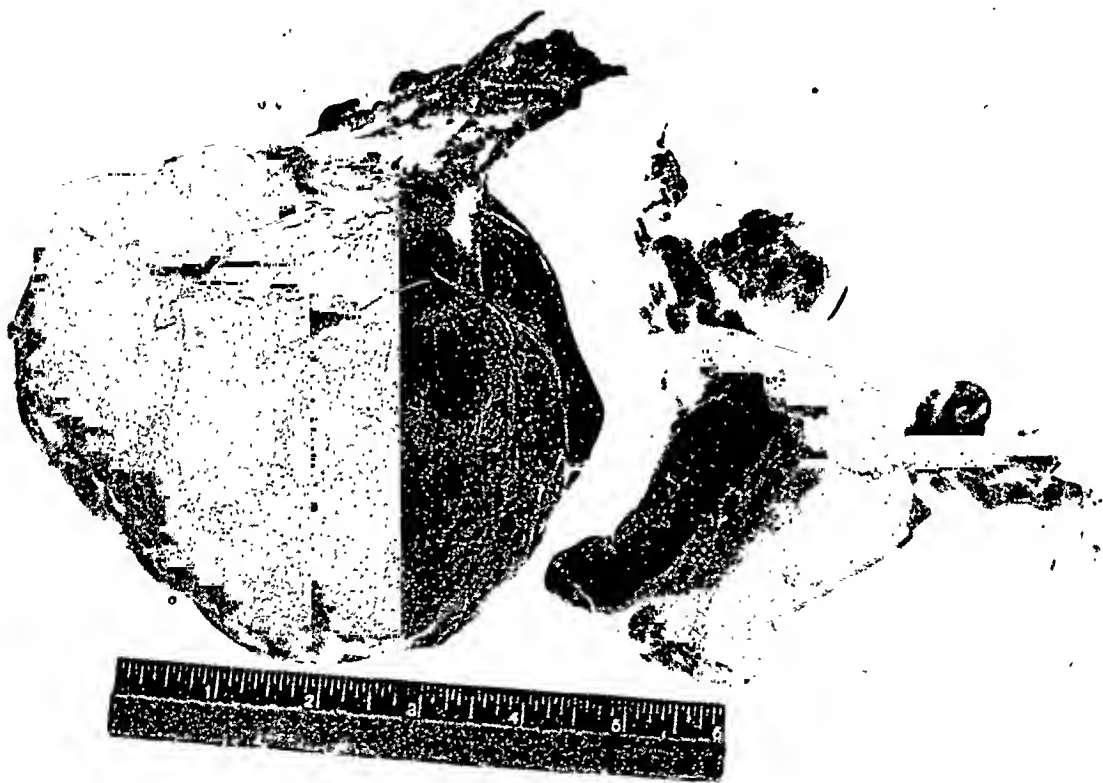


Fig. 1.—At left, the fibroma; at right, uterus (opened anteriorly) with attached tubes and ovaries.

The gross specimen was an eneapsulated mass measuring 15 cm. in greatest diameter, irregularly rounded with secondary projections from its surface. Sections through the mass disclosed large areas of whitish semi-solid gelatinous tumor and multiple cystic spaces, two of the latter being quite large (4 by 5 cm.). The cavities contained odorless, yellow, slightly mucoid fluid which coagulated upon standing. Uterus, tubes, and ovaries were grossly normal aside from the enlarged cervix and a small physiologic cyst in each ovary. Multiple microscopic sections through the tumor showed masses of well-differentiated connective tissue cells, large areas of edema and some hyalinization. The endometrium showed changes characteristic of the second or third



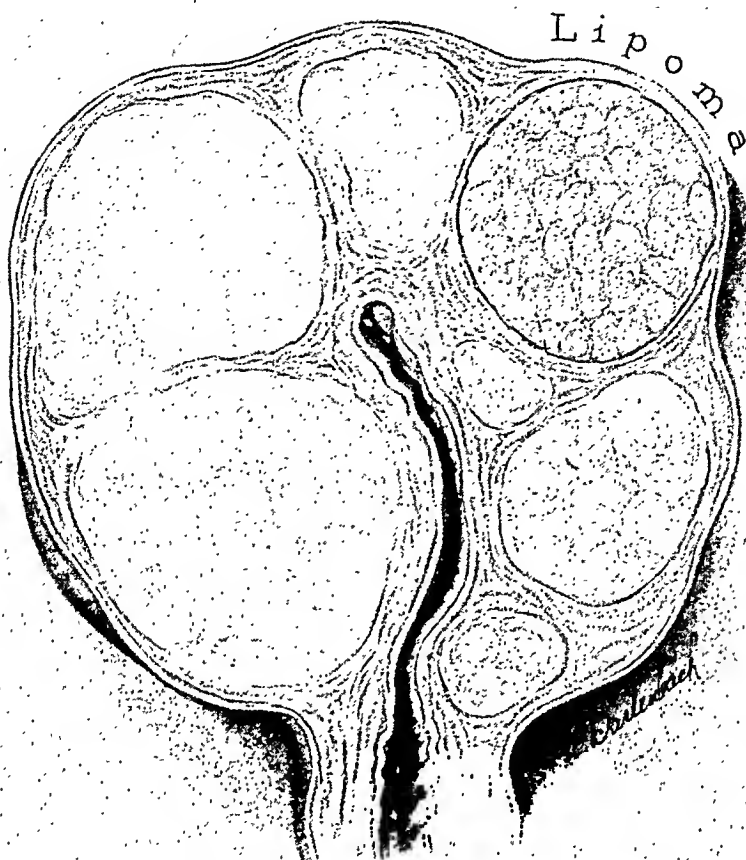


Fig. 1.—Cross section of uterus showing site of lipoma.

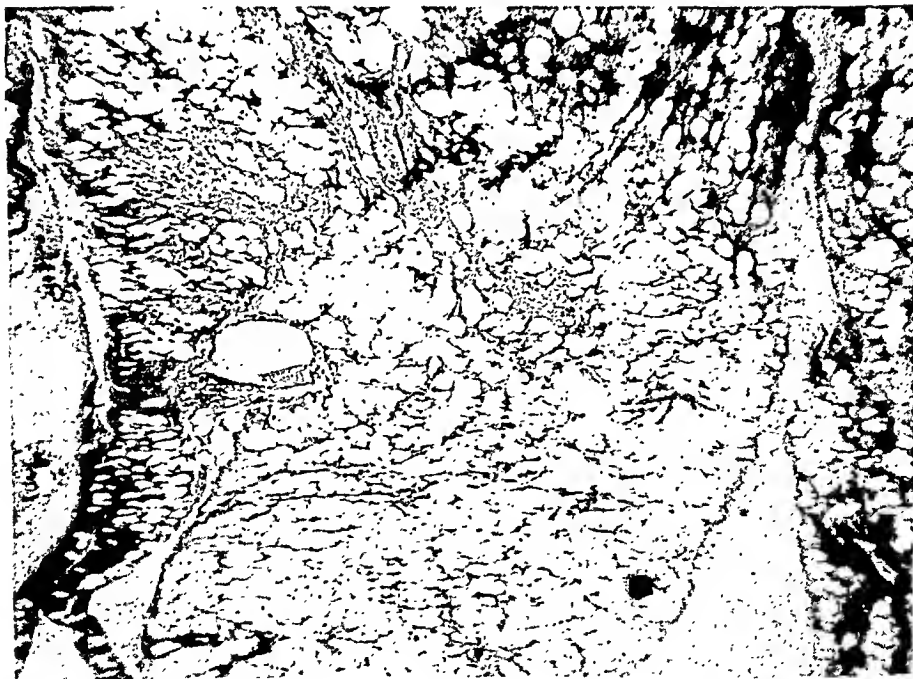


Fig. 2.—Photomicrograph of section of lipoma ( $\times 25$ ).

## PRIMARY LIPOMA OF UTERUS

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**B**ECAUSE this condition is extremely rare, and because it simulated a degenerating fibroid or a possible associated intrauterine pregnancy, we felt this case worthy of report.

In 1899 Brüning published for the first time a case of intramural lipoma of the uterus. Walkoff, in 1901, described in the German literature a case of sarcomatous degeneration of a uterine lipoma. In a review of the literature, D. P. Hall<sup>1</sup> quotes Ellis of London and Gault of Vienna, who analyzed 7,000 uterine neoplasms and found only four cases; two were fibrolipomas and two were small lipomas. F. B. Lund,<sup>2</sup> in his report, states that "they occur almost always in women over 60 years of age."

However, our own case report deals with a woman who was only 39 years of age.

Ritter and Stringer<sup>3</sup> reported a case of lipoma of the uterus in a patient 55 years of age.

A. J. Peterson,<sup>4</sup> in his review of mixed tumors of the uterus, lists a number of fatty tumors of the uterus which appeared in world literature ranging from the years 1816 to 1921, and only twenty-six lipomas are recorded.

The exact origin and pathogenesis of the uterine lipoma remains a moot problem. The rarity of the lipomas in the uterine wall may be ascribed to the lack of fatty cells in the muscle wall. Knox of Harvard, according to Ritter and Stringer, believes that the lipomas originate from embryonic cell rests, while Brüning believes that they are the transformation of the muscle fiber into fat. Others think that the fat cells around the blood vessels of the uterine wall may be the source of the lipoma. A. J. Peterson, whose histopathologic report scrutinizes every tumor carefully and fully, believes that grossly a tumor may appear like a lipoma, but that microscopic sections may reveal other tissue mixed with the predominating tissue.

### Case Report

B. O. (4518072), a 39-year-old Negro woman, gravida i, para i, was admitted to the Cook County Hospital with a history of a progressively enlarging abdominal tumor. She also complained of menorrhagia.

Physical examination revealed a woman who was not acutely ill. Her blood pressure was 150/90; temperature, 98.6° F.; pulse, 80.

The essential findings were those of a large abdominal mass the size of an eight months' pregnancy. It was firm and fixed.

Pelvic examination revealed no gross external genital abnormalities. The cervix was wedged against the symphysis pubis. The abdominal mass also filled the entire pelvis. Some areas of the mass felt quite soft, resembling a degenerating fibroid or a concomitant pregnancy.

A diagnosis of uterine fibromyoma was made preoperatively.

*Laboratory Data.*—The urine was negative; hemoglobin, 80 per cent; red blood count, 4,100,000; white blood count, 6,350. X-ray plate showed no fetal parts or other shadows.

## ABDOMINAL PREGNANCY WITH PLACENTA ATTACHED TO THE SPLEEN\*

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**A**BDOMINAL pregnancy at term is no longer a clinical rarity. Cornell and Lash reviewed the literature in 1933 and found that the maternal mortality was 14.3 per cent and the total infant mortality was 67.3 per cent. Only 35 per cent were diagnosed correctly before operation.

A review of the literature reveals no case in which the placenta was attached to the spleen in its entirety and it is for this reason that this case is being reported.

Mrs. S. G., a 35-year-old white married woman was referred to one of us (D. H. K.) on Sept. 6, 1944. Her last menstrual period began on June 6, 1944, and her estimated date of confinement was March 13, 1945. This was her third pregnancy. Both previous pregnancies were terminated by normal deliveries, in 1932 and 1935. Menstruation started at the age of thirteen, lasted five days, occurred regularly every twenty-eight days, and was painless.

She presented the following history: There was a bloody discharge for a two- or three-hour period three weeks after her last period in June. During July and August she "felt faint" most of the time, but more so toward evening. There was usually a feeling of pressure on the bladder and pain in the lower abdomen which was relieved by enemas.

About the middle of July she felt a severe pain in the left side, which spread over the entire abdomen, to the back, chest, and shoulders. She was unable to urinate or defecate, and laxatives had no effect. Enemas could not be taken because "the water refused to go in beyond a certain place." She had to be catheterized and this decreased the pain.

She was in bed for two weeks with the above complaints, taking codeine and "other drugs" daily. Urination and defecation were painful with tenesmus. She fainted frequently, especially when the bladder became full.

The backache was present all the time, more so on the left side. She had the sensation "as though the urine did not flow freely from the left kidney." There was also a constant ache in the left lower extremity, as well as occasional spotting.

Physical examination revealed no abnormalities except a mass in the right adnexal region. The uterus was enlarged to the size of a three months' pregnancy. Pelvic measurements were within normal limits.

*Laboratory Findings.*—Friedman test was positive and her blood was Rh positive. Wassermann test and urinalysis were negative. Basal metabolic rate was plus 2 per cent; hemoglobin, 65 per cent; red blood cells, 3,340,000; white blood cells, 9,950, with 63 per cent polymorphonuclear leucocytes, 32 per cent lymphocytes, and 5 per cent eosinophiles.

Weight on the first visit was 130 pounds, and during the first three months she gained 8 pounds, but this gain was lost during the last six weeks. Blood pressure ranged between 112/70 and 120/80. On two occasions she fainted in the office, but was able to go home alone. The fetal heart was heard until Feb. 12, 1945. X-ray on Feb. 14, 1945, revealed the following:

\*Presented at a meeting of the Washington Gynecological Society, November 24, 1945.

On May 5, 1945, three days after the admission to the hospital, she was operated upon. When the peritoneal cavity was entered, a large multinodular fibroid uterus was noted. However, one of these large nodes felt very soft on gross palpation. A supracervical hysterectomy and bilateral salpingo-oophorectomy was done. The patient made an uneventful recovery and left the hospital twelve days later.

*Pathological Report.*—Multiple uterine fibromyomas. One intramural encapsulated large lemon-sized node on cut surface appeared yellow and soft. Microscopic section revealed uniform areas of encapsulated fat; no mixture of muscle fibers.

*Diagnosis.*—Lipoma of uterus.

### Summary

In a review of the literature it appears that during the last twenty-five years only four cases of uterine lipoma are recorded. Review of literature by A. J. Peterson revealed only 26 lipomas on record from 1816 to 1921.

Although the lipoma, as such, is of no great importance, it is interesting from the didactic and histopathologic picture; and, clinically, its softness resembles a degeneration of a fibroid or a possible associated pregnancy.

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# INFREQUENCY OF CARCINOMA OF THE UTERINE CERVIX AMONG JEWISH WOMEN

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THAT carcinoma of the uterine cervix occurs with striking infrequency in Jewish women has been brought forth previously in several statistical studies and reports.<sup>1-5</sup>

In a recent analysis of 568 consecutive cases of carcinoma of the cervix encountered at the Mayo Clinic in the years 1938 to 1942, inclusive, and in which the diagnosis was proved at biopsy, it was found in 566 instances that the expressed religious preference of the patient was specifically given as other than Jewish. The religious preference was taken to be equivalent to what sometimes is designated as race. In not a single instance was the religious preference stated as being Jewish. There were two instances in which it was impossible to classify the patient definitely as Jewish or non-Jewish since the religious preference was given by the patient as "none, or no preference."

In a small number of the 566 cases, in which it would have been otherwise impossible to be sure, it was by the cooperation of the referring physician that it became definitely possible to classify the patient as non-Jewish; in the two doubtful instances mentioned, the referring physician was unable to help in definitely determining whether the patient was Jewish or non-Jewish. However, it can be definitely stated that in neither instance did it appear at all likely from the other available data that either of these two patients was Jewish. The impressive fact stands out that even if the two patients had been proved to have been Jewish, still the low incidence of Jewish women among patients with carcinoma of the uterine cervix would have been strikingly corroborated by this study. The estimated Jewish registration by per cent of total at the Clinic is approximately 7 to 8 per cent; the per cent of Jewish persons in the total population of the United States, as given in the World Almanac for 1945, is about 4 per cent.

It is quite possible that one or more Jewish women of Christian religion have been encountered in this series without our knowing that they were Jewish, since it is estimated that about 4 per cent of the Jewish population, or 200,000, are Christians.

On the basis of the 7 per cent mentioned in a preceding paragraph, one would have expected to find approximately forty Jewish women in our series; actually, as has been shown, there were no women in the group who were known to be Jewish and only two instances in which the religious and racial status of the patient was in doubt.

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*Roentgen Findings.*—Examination of the abdomen in the anteroposterior, oblique, and lateral positions revealed a fetus of about eight months' gestation in the left occipitoanterior position. The entire fetus did not give a normal tone; it was doubled upon itself somewhat, although the head did not present the Spaulding sign. Nevertheless, it was our belief that the fetus was non-viable.

The patient was admitted to Columbia Hospital on April 9, 1945, for a laparotomy on April 10, 1945. Under avertin and ethylene anesthesia, a mid-line suprapubic incision was made. Upon entering the peritoneal cavity, thin, dark, chocolate colored fluid and old blood escaped. A macerated fetus was extracted. The placenta was attached in its entirety to the spleen which was enlarged about four times its normal size and extended about six centimeters below the left costal margin. The placenta was removed very easily. The wall of the pregnancy was anterior to and covered all of the pelvic and abdominal viscera except for the spleen.

*Pathologic Report.*—The body was that of a badly macerated fetus without genitals,  $15\frac{1}{2}$  inches in length. The legs were badly deformed and extremely short, measuring only  $3\frac{1}{4}$  inches in length. The feet were of normal length but very flat. The anus was not perforated. All the abdominal structures were in a thin-walled membranous sac approximately 4 by 4 inches without apparent skin. The cord was  $6\frac{3}{4}$  inches long, and there was apparently no umbilicus. The placenta was  $6\frac{1}{4}$  by 4 by 2 inches.

The patient made an uneventful recovery, being discharged on the eleventh postoperative day. The highest temperature was  $102^{\circ}$  F. the night of the operation.

The first postoperative visit was on May 11, 1945, at which time the patient weighed 115 pounds, her temperature was  $101^{\circ}$  F. and a hard mass could be felt 2 cm. above the umbilicus. On pelvic examination, this mass was apparently attached to the uterus. The spleen was only slightly enlarged. On June 1, 1945, the mass was smaller and the temperature was  $99.4^{\circ}$ . On July 2, 1945, the mass was the size of a grapefruit. The patient was afebrile. On September 11, 1945, the mass was of the same size, patient had no fever, she weighed  $120\frac{1}{2}$  pounds and was able to go back to work. Menses had returned normally.

### Summary

A case of abdominal pregnancy with the placenta attached in its entirety to the spleen is reported. The fetus was abnormal and macerated. The mother made an uneventful recovery.

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# WINGED STEM PESSARY TO CORRECT STENOSIS OF CERVIX

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**S**TENOSIS of the external os uteri is occasionally met in sterility cases. This usually is the result of previous cauterization, but sometimes appears congenital. A probe will not pass the stenosis and, because of faulty drainage, the secretions become changed to the point that sperm will not progress through the canal.

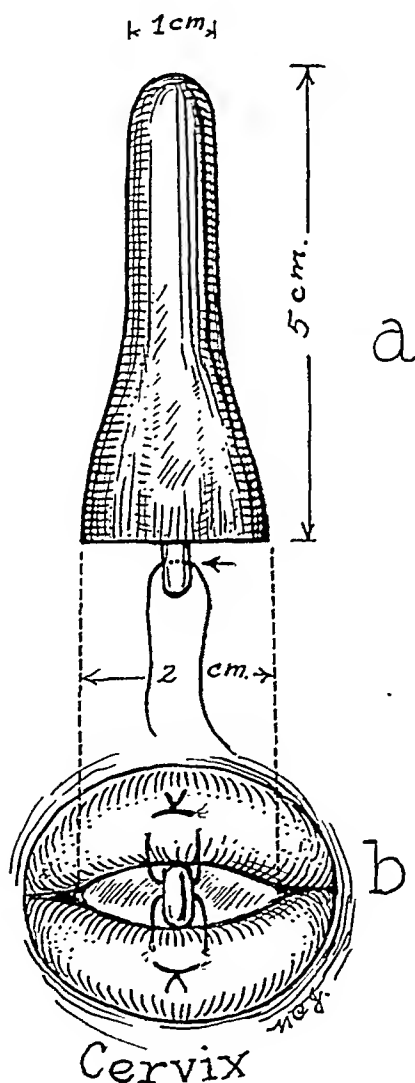


Fig. 1.

Various surgical procedures have been employed to overcome this difficulty, the simplest being posterior discission and the glass stem pessary. The cutting operation leaves a mutilated cervix, and the failures of the stem pessary gave me the idea of placing a wing on opposite sides of the cervicel end of the stem.

# MULTIPLE PREGNANCY WITH EARLY ABORTION OF ONE FETUS

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DELEE<sup>1</sup> mentions that in dichorionic or double-ovum twins, one fetus may die and be expelled, with the other going normally to term.

On Nov. 30, 1944, one of us (E. M. B.) was called to attend a young primipara who had undergone an abortion. By an examination of the products of conception, an embryo measuring approximately 6 cm. was identified. Vaginal examinations four weeks and again seven weeks later revealed a persistent enlargement of the uterus, first about the size of an orange, and later about the size of a grapefruit.

Nine weeks after the abortion occurred it was possible to identify positively fetal heart sounds and to recognize an enlargement of the uterus to about that of a four and one-half months' pregnancy. The case continued through a normal pregnancy to delivery on June 27, 1945, of a normal, full-term 7-pound male infant.

Apparently this is an instance of a multiple dichorionic pregnancy, in which one embryo was lost by abortion while the other progressed normally to term. Hirst<sup>2</sup> points out that many multiple pregnancy miscarriages occur but are overlooked.

In an analysis of 573 cases of twin pregnancy by Guttmacher<sup>3</sup> on the Johns Hopkins Hospital Service, no reference to such an occurrence is made. Similarly, Hirst's study of 305 twin pregnancies omits the details on any similar instance. If, however, the dead fetus is retained instead of being expelled early in pregnancy, the familiar fetus papyraceus results, and this is more frequently the subject of case reports.

Closer observation and more detailed histories on obstetric patients would lead to a more frequent recognition of early miscarriages in multiple pregnancies. DeLee mentions a specific case: "The senior author delivered a woman at term of twins, and she stated that five months previously she had had an abortion of four months." No doubt in the memories of many practitioners such an occasional history can be recalled. Case reports, however, are not numerous in medical literature.

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# Department of Reviews and Abstracts

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## Selected Abstracts

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### Pregnancy: Physiology, Diagnosis, Etc.

Lund, Curtis J.: Nutrition in Pregnancy, J. A. M. A. 128: 344, 1945.

The author reviews the essential dietary needs during pregnancy. He feels that for optimal supply the daily diet should consist of one generous serving of meat including liver weekly, one quart of milk, an ounce of butter, one fresh vegetable, one green leafy vegetable, and one other cooked vegetable, generous amounts of citrus fruits or their equivalent, an egg, and whole grain cereal or enriched bread. The average pregnant woman requires about 2,500 calories per day during pregnancy. For purposes of weight reduction, the diet may be limited to 2,000 calories or less, and minerals and vitamins may be supplemented. The diet should be ample in protein. There is no need for supplements in calcium if the patient gets one and one-half grams of native calcium daily. A daily intake of 15 mg. of iron will produce a positive balance in most cases, and in cases of iron deficiency 15 grains of ferrous iron daily will suffice. Most iron deficiency anemias occur in the last trimester of pregnancy. Plasma levels of vitamin A tend to decrease during pregnancy. Adequate amounts of the B complex can be supplied by diet alone. It is not necessary to give additional amounts of vitamins C and E during pregnancy. Complications of pregnancy probably exert a greater influence on nutrition than does nutrition on them. Such conditions as hyperemesis gravidarum, pyelitis of pregnancy, puerperal infection, and other acute and chronic infections may produce nutritional deficiencies.

WILLIAM BERMAN.

Odell, Lt. Lester D., and Mengert, Wm. F.: The Overweight Obstetric Patient, J. A. M. A. 128: 78, 1945.

The authors found 641 cases of obese women (weighing 200 pounds or more at or before birth of a potentially viable baby). The incidence of obese women was 3.85 per cent, and the incidence of deliveries among obese women was 4.57 per cent. Fourteen sets of twins were encountered, which is somewhat higher than the normal incidence of twinning. Toxemia of pregnancy was noted in 31.4 per cent of the cases, and the next most frequent finding was glycosuria. These women tend to be relatively young and fertile. No unusual presentation was noted in these women. Prolonged labor (30 or more hours) occurred in 5 per cent of the cases. Postpartum hemorrhage was noted in 7.1 per cent of the cases. The operative incidence is approximately twice the usual clinical incidence. Approximately 57 per cent of the infants weighed more than 3,500 grams at birth. Thirty-five of the infants died (4.5 per cent). Forty-three per cent of the fetal deaths occurred in utero. Puerperal complications, chiefly sepsis, occurred in 12.6 per cent of the cases. There were four maternal deaths (0.53 per cent). It was noted that with repeated pregnancies the incidence of hypertensive disease, fetal death, breech, and occiput posterior presentation increased.

WILLIAM BERMAN.

This winged pessary is placed in the cervix after an incision is made in the cervicæal canal on both sides from the internal os in a slanting, outward direction to the lateral edge of the external os. Usually, it is wise to dilate the canal first. When inserted, the wings of the pessary fit into the bilateral cunts, separating the surfaces so that the epithelium grows in over the raw edges. Healing takes place in about two weeks, leaving a funnel-shaped opening which looks like a bilateral first-degree tear. The pessary should be anchored to both the anterior and posterior lips with a mattress suture of silkworm gut.

This winged stem pessary has been used only in highly selected sterility cases on whom all other tests have been normal except the Hühner test. While only twelve patients have been so treated in the last six years, eight have become pregnant.

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come, and points out what may have been done to avoid it. The patient was a 27-year-old Negro nullipara who, according to her story, had had a sudden bloody vaginal discharge and severe lower abdominal pain following a two-month interval of amenorrhea. On admission to the hospital, a diagnosis of twisted ovarian cyst and pelvic inflammatory disease was made. Operation was performed on the eighth day following admission at which time there was marked abdominal distention and a rising temperature. A five months' fetus was found in the peritoneal cavity surrounded by its amniotic sac which had been extruded through a longitudinal rent in the posterior wall of the uterus. The abdomen also contained a large quantity of liquid blood and many clots. The edges of the uterine laceration were necrotic, partially organized, and showed adhesions to ilium and omentum. In view of these findings, a rapid supravaginal hysterectomy was performed, but the patient went into deep shock and expired forty minutes following the conclusion of the operation.

It is obvious that interference in order to induce abortion had occurred, which accounted for the laceration of the uterus, and that the patient's persistent denial did much to confuse the picture. However, in the author's opinion, the diagnosis should have been made and operation performed much earlier. The importance of combating shock is also stressed.

FRANK SPIELMAN.

### Puerperium

Vignes, H.: Postpartum Phlegmasia Without Fever or Permanent Tachycardia, *Rev. de path. Comparée*. 553: 38, 1940.

The author reports the case of a primipara who had an uneventful pregnancy except for varicose veins and a mild albuminuria. She had a quick, easy labor, and the puerperium was entirely afebrile. However, on the tenth day, the calf of the left leg was painful, tender to the touch, swollen, and violet in color. There was pain at the bend of the groin and along the crural vein. During the following few days the edema increased considerably. In spite of these findings, both the temperature and pulse remained normal. The attack of phlebitis lasted twelve days and the symptoms disappeared after two months.

This case emphasizes what the author has previously maintained that even normal easy labor may be followed by phlebitis. Therefore, the discussion should be reopened as to whether or not phlebitis always has a microbial origin, as maintained by many obstetricians. The author believes that the case he reports most likely did not have an infectious basis.

J. P. GREENHILL.

Trivelli, O., and Garcia, P.: Pelvic Puerperal Suppuration Spontaneously Opened Into the Rectum, *Bol. Soc. chilena de obst. y ginec.* 9: 161, 1944.

The authors have observed ten such cases in slightly over one year. Their occurrence must be higher than commonly supposed and their diagnosis is seldom made because the physician does not think of them.

The pathognomonic sign is sudden evacuation of a large amount of pus with the feces; this is nearly always followed by termination in crisis of the signs of suppuration. This "rectal emesis" is preceded by a characteristic symptomatology which must be correctly interpreted. It consists of diarrhea, rectal tenesmus, pain in the perineum, bladder symptoms without urinary infection, together with the classical symptoms of suppuration.

There were two postpartum and eight postabortion cases.

The various types of pelvic suppuration may give rise to the accident such as phlegmon of the broad ligament, tubo-ovarian abscess, suppurative parametritis and adnexitis, pelvic cellulitis, etc.

Evacuation of the pus through the rectum occurred from six to eleven months after delivery or abortion. The evolution was most rapid in the two postpartum cases.

Perez, Manuel Luis: *Diagnosis of Anencephaly During Pregnancy*, An. d. Inst. matern. y asist. social, Buenos Aires 5: 86, 1943.

The author insists that a clinical diagnosis of anencephaly may be arrived at on the basis of the following facts: difficulty in locating the cephalic pole in the small pelvis, when no other factors exist to account for it; identification of the pelvic pole at the opposite end and provocation of fetal movements, even convulsions, by compression of the zone which logically should be occupied by the lower pole. Roentgenography will confirm the suspected anomaly.

J. P. GREENHILL.

### Pregnancy: Complications, Etc.

Polayes, S. H.: *Erythroblastosis Fetalis in Mothers With Rh Positive Blood (Report of 6 Cases With Comment on Isoimmunization With the A and B Agglutinogens)*, Am. J. Dis. Child. 69: 99, 1945.

The author reports two cases which fulfill all the clinical criteria for the diagnosis of erythroblastosis fetalis (icterus gravis neonatorum).

In both cases the mother's blood group was group O, Rh positive and the child's group A, Rh positive. The Rh factor and all its known variants, as well as the Hr antigen, were excluded as possible immunizing antigens. Although more statistical data are required to establish the frequency of such cases, nevertheless it is believed that (a) isoimmunization by the A and B agglutinogens may occur, and that (b) erythroblastosis fetalis may result from A or B isoimmunization by a mechanism similar to that already established for the Rh factor.

JAMES P. MARR.

Gregg, N. McAllister: *Rubella During Pregnancy of the Mother With Its Sequelae of Congenital Defects in the Child*, M. J. Australia 1: 313, 1945.

The author reviews the historical development of the sequelae of rubella with relation to congenital defects of the newborn. These consist chiefly of congenital defects of the eyes, ears, teeth, and heart. This disease is important from the standpoint of public health. The author urges everyone to consider this complication of pregnancy as serious and urges study of the disease with an attempt to isolate the virus and develop both a prophylactic and a curative treatment. It is felt that careful and detailed evaluation and investigation of the maternal history throughout pregnancy may unravel some of the unsolved problems with reference to congenital defects.

WILLIAM BERMAN.

Fox, M. J., and Sennet, L.: *Poliomyelitis in Pregnancy*, Am. J. Med. Sci. 209: 382, 1945.

Case histories of four pregnant women who developed anterior poliomyelitis are presented. From a review of the literature, the conclusion is reached that pregnancy increases the susceptibility to poliomyelitis. Of the cases reported in adult women 31.3 per cent were pregnant. The increased susceptibility may possibly be due to the change in the ovarian secretion, although pituitary dysfunction as well as fetal hormones may also be factors.

In the four cases reported, the delivery of two normal children and the examination of a fetus in a dead mother confirmed the opinion that poliomyelitis in the mother does not affect the newborn child, nor does it hamper normal spontaneous delivery. Possible studies on the endocrinologic approach to the poliomyelitis problem are suggested.

FRANK SPIELMAN.

Badia, P. D.: *Instrumental Rupture of a Five Months' Pregnant Uterus*, Am. J. Surg. 66: 97, 1944.

Early diagnosis and immediate surgical intervention is recognized as being of paramount importance in the management of the ruptured pregnant uterus. In presenting this case report, the author in retrospect analyzes the factors which resulted in the fatal out-

provement during which plasma therapy with sulfathiazole was administered every other day. After the second episode, there was again a remission of symptoms for one day, followed by another aggravation which lasted only five days and coincided with the administration of 275,000 units of penicillin, at the rate of 25,000 units daily. Then came a period of improvement for nine days, interrupted by the appearance of a pulmonary abscess with its septic picture which improved as soon as the collection of pus emptied into a bronchus.

The insufficient dosage of penicillin and the fact that the only organism found in cultures of the lochia was *Escherichia coli hemolytica*, which is penicillin-resistant, would suggest slight or no action of the drug in this case. But the failure of sulfonamide therapy, blood transfusions, and sulfonamide plasma therapy during the first two episodes, and the occurrence of improvement as soon as penicillin was used militate in favor of a beneficial action of the drug. Besides, the presence of *Escherichia coli* in the lochia does not mean that the general infection of the patient was caused by this germ.

The second case was supposed to be a thrombophlebitis of the upper pedicle: apparently it improved with the first course of penicillin, because the septic picture returned on suspension of the drug and definitely improved with the second course which was followed by sulfadiazine therapy. Altogether, 710,000 units of penicillin were given intramuscularly. During the second course, four blood transfusions were also given to combat co-existing anemia and as adjuvant treatment.

J. P. GREENHILL.

### Vaginal Infections

Sako, Wallace, Tillbury, Ross, and Colley, Jesse: One-Dose Penicillin Treatment of Chronic Gonorrheal Vaginitis in Children, J. A. M. A. 128: 508, 1945.

The authors report 16 cases of chronic gonorrheal vaginitis treated by the one-dose method. In all clear-cut cases the diagnosis was established by smear, and in other cases the diagnosis was made by smear and culture. After all previous medication had been discontinued for one week, the patient was given 100,000 units of penicillin dissolved in 20 c.c. of isotonic sodium chloride solution. This was injected intramuscularly. In some cases 3 minims of adrenalin were added to prolong the effect. A cure was effected in 15 of the 16 cases treated. No toxic symptoms were noted and hospitalization was not necessary.

WILLIAM BERMAN.

Carceller, Mariano Vicente: Trial of Sulfonamide Therapy in a Case of Vulvar Condylomatosis, Rev. españ. de obst. y ginec. 1: 183, 1944.

The author prescribed tentatively a para-amido-phenyl-sulfamide ointment for local application to the cleansed lesions. After one week he observed marked improvement: some of the vegetations of the upper and central portions of the principal seat of the lesions had disappeared completely and others were evidently regressing. After two weeks of treatment, only a few condylomas were left in the region of the fourchette and these were smaller and definitely improved. Cure was undoubtedly completed with continuation of the treatment, but this could not be demonstrated because the patient did not return.

J. P. GREENHILL.

Schauffler, Goodrich C., and Schauffler, Caroline: Current Concepts of Vaginitis and Vulvar Irritations in Infants and Children, West. J. Surg. 53: 35, 1945.

Irritation of the vulva in children may be the result of simple neglect, long contact with urine or feces, allergic tendencies, trichomonas and monilia infection, trauma secondary to masturbation, diabetic dermatitis, and pin worms. Actual infections of the vulva in children is rare. Practically all infections of the vulva were secondary to infections of the vagina, and approximately 60 to 70 per cent of the infection in the vagina is caused

All cases healed well and subsequent, repeated proctoscopy could not demonstrate a fistulous opening. In most cases there was a complete return to normal; in the others there persisted a residual process characterized by induration on palpation and a higher sedimentation rate, but without subjective manifestations worthy of consideration.

When opening into the rectum becomes imminent, in the presence of a grave toxic picture with evident danger, it may be advisable to help evacuation through the rectum with the object of eliminating as soon as possible the cause of the toxemia which may kill the patient. If spontaneous evacuation is incomplete, proctoscopy to locate the orifice, enlarge it, and obtain better drainage may be advisable.

J. P. GREENHILL.

Thompson, J. W., and Le Blanc, L. J.: Congenital Diaphragmatic Hernia, *Am. J. Surg.* 67: 123, 1945.

Following spontaneous delivery of a normal infant, the patient, whose case is here reported, a gravida ii, suddenly experienced severe epigastric pain five hours after parturition, and showed signs of marked distress referred to the chest. In addition to the usual supportive measures instituted, bedside x-ray revealed the stomach displaced into the left thorax. A diagnosis of left diaphragmatic hernia with strangulation was made and, because of the continued alarming condition of the patient, laparotomy was decided upon. At operation most of the hollow abdominal viscera were found to have migrated into the left chest through a large opening in the diaphragm. The mesenteries of the stomach and intestine were elongated, and there was counterclockwise rotation of the viscera causing torsion of the pancreas which was acutely inflamed and covered with a fibrinoplastic exudate with numerous areas of fat necrosis. The only organs remaining in the abdomen were the spleen, the liver, and the descending colon. The viscera were easily replaced, the margins of the hernial ring freshened with scissors, and approximated and overlapped with one layer of chromic catgut and another of heavy black silk. With the aid of parenteral glucose-saline and small transfusions, the patient made a good recovery.

The literature is reviewed, and the authors, besides calling attention to the possibility of this condition which often remains undiagnosed, stress the importance of immediate surgical intervention as in any strangulated hernia. Where the diagnosis is made early in pregnancy, they favor immediate repair because of the grave danger of strangulation during the latter months or as a complication of delivery or of the puerperium.

FRANK SPIELMAN.

Trillat, P., and Notter, A.: Bacteriologic Study of Pyelonephritis Associated With the Puerperal State, *Gynec. et obst.* 40: 491, 1939.

The authors observed 60 cases of pyelonephritis, 37 of which began during pregnancy, and 23 began post partum. In 27 cases the colon bacillus was isolated; in 3 cases, staphylococci; and in 2 cases, the Friedländer bacillus; all in pure culture. In the remaining 28 cases there were mixed groups of bacteria. In 67 per cent of these 28 cases the colon bacillus was associated with the enterococcus. In others streptococci, staphylococci, and pseudodiphtheria were present. Among the 60 cases there were 13 cases of albuminuria. There were no maternal deaths in this series and only one fetal death. There were four premature babies in the entire group. The cases with pure strains of bacteria were less serious than those with associated organism. All the patients were treated with auto-vaccinotherapy and in no case was ureteral catheterization necessary.

J. P. GREENHILL.

Keymer, Eduardo: Two Cases of Grave Puerperal Infection Treated With Penicillin, *Bol. Soc. chilena de obst. y ginec.* 9: 287, 1944.

The author states that his first case, which he regards as one of chronic pyemia, presented two episodes of fourteen days each, which were treated with 66 and 57 Gm. of sulfadiazine, respectively. These episodes were separated by three days of relative im-

hysterectomy was easily performed. In one of the cases of natural delivery at term, Wertheim's operation was performed eight weeks later, and in the other, vaginal hysterectomy was done four months after delivery.

At the time of operation, all cases were within the limits of operability, and there was no operative mortality. Three patients were not heard from after the operation. Of the other three, one died after fourteen months and one after eight months, both from metastasis to the pelvis; the third is alive and well for over six years.

J. P. GREENHILL.

**Albertelli, Jorge F.: Cancer of Cervix and Pregnancy, Bol. Soc. de obst. y ginec. de Buenos Aires 23: 217, 1944.**

The author presents the rules followed at the Maternity Institute in the treatment of these cases.

**Operable cancer.** In a pregnancy over six months, abdominal cesarean section is performed and followed immediately by total hysterectomy. When the viability of the fetus cannot be established with certainty, expectation of not over three weeks may be adopted to increase the chances of fetal survival.

In a pregnancy under six months, total hysterectomy of the intact uterus is performed. In a pregnancy of from five to six months, application of radium (40 m.c.d.) may be used to allow waiting for growth of the fetus until it is viable.

During labor, abdominal cesarean section is performed, followed by total hysterectomy.

In inoperable cancer, in a pregnancy over six months, abdominal cesarean section followed immediately by Porro hysterectomy or simple subtotal hysterectomy is performed. Subsequently, intracavitary radium therapy and transeutaneous roentgen therapy are used. In borderline cases of fetal viability, an application of radium is given as mentioned for operable cancer.

In a pregnancy under six months, respect for fetal life must increase as the probabilities of ultimate cure of the mother decrease. Radium application (50 m.c.d.) is recommended. Early pregnancy will probably be interrupted; if not, interruption may be considered after cicatrization of the cervical lesions. If the pregnancy is close to six months, viability of the fetus will be awaited and the same conduct is then adopted as in pregnancy over six months. Once the uterus is evacuated, the treatment is completed with transcutaneous pelvic roentgen therapy.

During labor, the treatment is cesarean section followed by Porro hysterectomy and then physiotherapy.

The corrected operative mortality of Albertelli's series is 0 per cent, the death of one patient being due to an anesthetic accident.

J. P. GREENHILL.

by the gonococcus. The low estrogen concentration in the immature female results in a thin vaginal membrane, and its pH is such as to encourage the bacterial growth. The cervix does not harbor infection. It may be the site of erosions due to extrusion of the delicate, single-layered, endocervical mucosa. No treatment is indicated.

Vaginitis and secondary vulvitis in children is satisfactorily treated by the local use of estrogen suppositories and sulfathiazole. The vulva is washed with a cleansing solution, and if local administration is difficult, the sulfonamides may be given by mouth. Resistant gonococcal infection can be treated by the use of penicillin.

Foreign bodies in the vagina produce an acute vaginitis, but the discharge is usually blood-tinged. Exploration with a sound will elicit contact sensations which aid in the diagnosis.

WILLIAM BICKERS.

### Venereal Diseases

Gray, Laman A.: The Treatment of Acute Gonococcal Pelvic Inflammatory Disease in the Female With Penicillin, *South. M. J.* 38: 405, 1945.

The author reports on the treatment of thirteen women with gonococcal pelvic inflammatory disease after treatment with penicillin. Each case had been diagnosed by culture on chocolate agar plates. Each patient received 25,000 units of penicillin intramuscularly every three hours for forty-eight hours, a total dose of 400,000 units. Patients were allowed out of bed. No ice bags or douches were given. All patients were bacteriologically cured as shown by smears and cultures. The symptoms of acute salpingitis and peritonitis began to improve forty-eight hours after the penicillin was begun. The cervical discharge changed from the purulent type to a mucoid discharge in three days. The tuboovarian masses and pelvic induration frequently progressed after the patient was apparently cured from a bacteriologic standpoint. Residual pelvic induration was found in all thirteen cases, in spite of the fact that they were bacteriologically cured.

WILLIAM BICKERS.

Day, Lois A.: Chaneroid of the Cervix: Report of Two Cases, *Proc. Staff Meet. Mayo Clin.* 20: 70, 1945.

Prior to the war, chaneroid was very rarely encountered except in seaport cities and in communities with a large Negro population. Since the war began, the author thinks it well to be on the lookout for chaneroid infection, particularly of the cervix, and for the purpose of calling attention to some of the clinical manifestations of chaneroid in the female, reports two such cases seen in the Mayo Clinic. The diagnosis is made by excluding syphilis, gonorrhea, the presence of the *Hemophilus ducreyi* in smears, and a negative Frei test. Chemotherapy: sulfathiazole very promptly cleared up the first case; but, in the second, the patient could not take the sulfonamide and penicillin was given with marked success.

HARVEY B. MATTHEWS.

### Malignancies

Rojas, Daniel A.: Cancer of Cervix and Pregnancy, *Bol. Soc. de obst. y ginec. de Buenos Aires* 23: 471, 1944.

The author reports six cases from which he draws the following conclusions:

Cancer of the cervix is an infrequent complication of pregnancy. Five of the patients were between 30 and 35 years of age, and multiparas. The diagnosis of cancer was made during labor and in the ninth, seventh, and fourth months of pregnancy in one case each, and in the third month in two cases.

In four cases the pregnancy went to term; in two of them the fetus was delivered through the natural route and in the other two by cesarean section, which was followed by total hysterectomy. In two cases of pregnancy in the third month, the Wertheim or Latzko



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## Reply by Dr. Hesselstine

To the Editor:

I appreciate the views of Dr. Silbernagel and Dr. Burt, and support their right to clarify their views. I question not their results, but the mode of action which gave these results. We did not use the intravenous method as advised by Silbernagel and Burt, for we do not know of any pharmacological proof that the intravenous route is distinctly superior to the intramuscular route.

Our primary concern was for proof, not contention. We extend the request for compilation of facts and adequate controls in all scientific studies.

H. CLOSE HESSELTINE, M.D.

CHICAGO LYING-IN HOSPITAL

## The Guterman Pregnancy Test

To the Editor:

The May, 1946, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY (Vol. 51, pp. 685-691) includes a paper by A. G. Morrow and R. S. Benua entitled, "An Evaluation of the Guterman Pregnancy Test." These authors set out to test the validity of the color method of pregnanediol determination as a diagnostic test for pregnancy in a study of 19 patients. The original procedure was reported in two papers (*J. Clin. Endocrinol.* 4: 262-267, 1944; 5: 407-411, 1945), the conclusions being based upon an examination of 248 cases. The details of the method and its basis are given in extenso there. This work has been completely confirmed in 304 cases by G. McCormack (*AM. J. OBST. & GYNEC.* 51: 722-725, 1946), who followed the technique closely.

I should like here to point out the reasons which I think led to the contradictory results reported by Morrow and Benua in their small series.

1. The "slight modifications for convenience" are neither slight nor are they convenient for clinical laboratory use. These modifications include vacuum distillation over a steam bath instead of evaporation on the hot plate, the use of 1 ml. of a 10 per cent solution of sodium in 95 per cent ethanol instead of 20 ml. of a two per cent solution of sodium hydroxide in absolute methanol, and the use of No. 42 Whatman paper instead of fritted glass filters.

2. The authors adapted the qualitative color test to a Klett colorimeter employing a filter transmitting between 500 to 570  $m\mu$ . At 500  $m\mu$  pregnanediol in concentrated sulfuric acid shows little color absorption. The maximal color absorption is between 420 to 430  $m\mu$  as reported by N. B. Talbot and co-workers (*J. Clin. Endocrinol.* 1: 668-673, 1941) and this laboratory (1944). That Morrow and Benua were not measuring pregnanediol alone is borne out by their inconsistent quantitative colorimeter readings upon the addition of pure pregnanediol to male urine. In this laboratory, the addition of pure pregnanediol to male urine leads to reproducible colorimeter readings (Klett-Summerson colorimeter, 420  $m\mu$  filter and Cenco-Sheard spectrophotometer, 430  $m\mu$  band) when the procedure is followed closely.

Since the method was not followed in important details, and since the colorimeter assay was done at a wave length which may include substances other than pregnanediol, the paper is strictly speaking not an evaluation of the test as published from this laboratory.

HENRY S. GUTERMAN, M.D.

DEPARTMENT OF METABOLIC  
AND ENDOCRINE RESEARCH  
MICHAEL REESE HOSPITAL  
CHICAGO, ILL.  
MAY 21, 1946

## Correspondence

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### Pyridoxine in Nausea and Vomiting of Pregnancy

*To the Editor:*

In his article (AM. J. OBST. & GYNEC. 51: 82, 1946) Dr. Hesseltine says that "pyridoxine in the dosages and methods used is of no more value in the treatment of mild or moderate nausea and vomiting of pregnancy than scores of other preparations." He also states that the use of pyridoxine in the "treatment of hyperemesis gravidarum is valueless and without justification." This last statement was made with the observation of one patient who did not respond to treatment as used by Dr. Hesseltine. We believe our answer to his conclusions given is that the pyridoxine was incorrectly administered.

His article casts doubt on the results obtained and reported by us on the use of pyridoxine in nausea and vomiting of pregnancy.<sup>1</sup> We should like to clarify the points upon which we disagree.

Dr. Hesseltine pointed out, quite rightly, that a plethora of products had been used, the virtues of many of them extolled, and the subsequent failures left unreported. We do not wish to retract, in any way, any of the statements made by us concerning the use of pyridoxine hydrochloride, as used by us, in the treatment of nausea and vomiting of pregnancy.

He stated that it was impressive that a number of patients with symptoms sufficient to require treatment could be collected in a short period of time. Since one-third of all pregnant women have nausea and vomiting to a marked degree, the number of patients is not difficult to explain. Our original article contained a report on the results of treatment of forty patients. From September, 1943, when our original report was made, through September, 1945, we gave prenatal care to and delivered eight hundred thirty private patients. Two hundred of these patients had symptoms producing discomfort or illness sufficient to require treatment. All of these patients fell into one of the four classifications suggested by Weinstein and his associates.<sup>2</sup> Three patients in this group were sufficiently ill to require hospitalization and, in addition to pyridoxine hydrochloride, the usual methods of treatment were employed. All recovered and were delivered at term. In the entire group there were three other patients who were not relieved by the use of pyridoxine hydrochloride.

Our objection to Dr. Hesseltine's conclusions are based on the fact that he condemned the treatment but did not follow the same procedure as used by us. We did not put patients on a schedule of treatment. We stated in our original article that we found oral therapy to be of no value. We did not give pyridoxine hydrochloride intramuscularly. All of our injections were given intravenously, the dosage being 25 to 50 mg., and repeated as often as the symptoms recurred.

We have found pyridoxine hydrochloride, given intravenously, a very highly satisfactory agent to be used in the treatment of nausea and vomiting of pregnancy. If at any time we find it necessary to reverse our opinion, we shall so inform the interested members of the medical profession.

WYNNE M. SILBERNAGEL, M.D.  
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# Item

## American Board of Obstetrics and Gynecology, Inc.

Candidates certified at the annual meeting of the American Board of Obstetrics and Gynecology, May 5 to 11, 1946:

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BRANINARD, HOLLIS H., Thomas-Davis Clinic, Tucson, Arizona  
BRAUN, GUSTAVE A., 24 Centre Street, South Orange, New Jersey  
BRIERTON, JOHN F., School of Naval Administration, Stanford University, San Francisco, California  
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CLINE, ABE, 6318 San Vincente Blvd., Los Angeles, California  
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CONNELL, JOHN N., 26 Carlton Avenue, Jersey City, New Jersey  
COOPERSMITH, BERNARD I., 116 S. Michigan Ave., Chicago 3, Illinois  
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DAVERSA, BENJAMIN, 219 Madison Ave., Spring Lake, New Jersey  
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- New Orleans Obstetrical and Gynecological Society. (1924) *President*, E. L. Zander. *Secretary*, R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.
- St. Louis Gynecological Society. (1924) *President*, Otto Krebs. *Secretary*, John E. Hobbs, 630 S. Kingshighway, St. Louis, Mo. Meetings second Thursday, October, December, February, and April.
- San Francisco Gynecological Society. (1929) *President*, Albert M. Vollmer. *Secretary*, Daniel G. Morton, University of California Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.
- Texas Association of Obstetricians and Gynecologists. (1930) *President*, T. F. Bunkley. *Secretary*, J. McIver, 714 Medical Arts Bldg., Dallas, Tex.
- Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, Robert B. Kennedy. *Secretary*, Milo R. White, 2799 W. Grand Blvd., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).
- Central New York Association of Obstetricians and Gynecologists. (1938) *President*, Edward C. Hughes. *Secretary*, Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.
- Alabama Association of Obstetricians and Gynecologists. *President*, Gilbert F. Douglas. *Secretary*, Hunter Brown, 1922 South Tenth Ave., Birmingham, Ala.
- San Antonio Obstetric Society. *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.
- Seattle Gynecological Society. (1941) *President*, Gerhard Ahnquist. *Secretary*, Roger E. Stewart, Stimson Bldg., Seattle, Wash. Meetings held on third Wednesday of each month.
- Denver Obstetrical and Gynecological Society. (1942) *Secretary*, Emmett A. Meehler, 1612 Tremont St., Denver, Colo. Suspended during war.
- Wisconsin Society of Obstetrics and Gynecology. (1940) *President*, Roland S. Cron. *Secretary*, Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.
- San Diego Gynecological Society. (1937) *President*, R. C. Hall. *Secretary*, D. Dalton Deeds, 2001 Fourth Ave., San Diego, Calif. Meetings held on the last Wednesday of each month.
- North Dakota Society of Obstetrics and Gynecology. (1938) *President*, Ralph E. Leigh, Grand Forks. *Secretary*, G. Wilson Hunter, 807 Broadway, Fargo, N. D.
- Virginia Obstetrical and Gynecological Society. (1936) *President*, A. L. Carson, Jr. *Secretary*, L. L. Schamburger, 628 State Office Bldg., Richmond, Va. Next meeting not announced.
- Columbus Obstetrical and Gynecological Society. (1944) *President*, Wynne M. Silber-nagel. *Secretary*, Zeph J. R. Hollenbeck, 9 Buttles Ave., Columbus, Ohio. Meetings held fourth Wednesday of each month.
- Nassau Obstetrical Society. (1944) *President*, George B. Granger. *Secretary*, William S. C. Dolan, 2870 Northern Blvd., Manhasset, N. Y. Meetings, bimonthly from October to May.
- Bronx Gynecological and Obstetrical Society. (1924) *President*, Harry Gordon. *Secretary-Treasurer*, J. Irving Kushner, 1840 Grand Concourse, New York, N. Y. Meetings, fourth Monday monthly from October to May.
- Washington State Obstetrical Society. (1936) *President*, John H. Fiorino, Everett. *Secretary*, H. H. Skinner, Yakima. Meetings, first Saturday of April and October.
- Kansas City Obstetrical and Gynecological Society. (1922) *President*, J. Milton Singleton. *Secretary*, Richard C. Helman. Meetings, third Thursdays, September, November, January, March, and May, University Club.
- Los Angeles Obstetrical and Gynecological Society. (1914) *President*, George E. Judd. *Secretary*, Carl E. Krugmeier, 2200 West Third Street, Los Angeles, Calif.
- North Carolina Obstetrical and Gynecological Society. (1932) *President*, Wallace B. Bradford. *Secretary*, Richard B. Dunn. Meetings semiannually.
- The Society of Obstetricians and Gynecologists of Canada. (1944) *President*, William A. Scott. *Secretary*, James Goodwin, 516 Medical Arts Bldg., Toronto, 5. Meetings held annually, date of next meeting to be announced later.

# ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES\*

(Appears in January, April, July, October)

- American Gynecological Society.** (1876) *President*, Norris Vaux, Philadelphia, Pa. *Secretary*, Norman Miller, Ann Arbor, Mich. Annual meeting to be announced.
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons.** (1888) *President*, Lewis F. Smead, Toledo, Ohio. *Secretary*, James R. Bloss, 418-11th Street, Huntington, W. Va., Annual meeting Hot Springs, Va., Sept., 1946.
- Central Association of Obstetricians and Gynecologists.** (1929) *President*, John H. Moore, Grand Forks, N. D. *Secretary-Treasurer*, W. F. Mengert, Dallas, Tex. Annual meeting Chicago, Ill., Sept. 19-21, 1946.
- South Atlantic Association of Obstetricians and Gynecologists.** (1938) *President*, Robert A. Ross, Durham, S. C. *Secretary*, T. J. Williams, University, Va. Annual meeting on steamer, Tampa to Havana, Feb. 7-8, 1947.
- A. M. A. Section on Obstetrics and Gynecology.** *Chairman*, Philip F. Williams, Philadelphia, Pa. *Secretary*, William Mengert, 2211 Oak Lawn Ave., Dallas, Tex. Annual meeting San Francisco, July 1-7, 1946.
- New York Obstetrical Society.** (1863) *President*, Harvey B. Matthews. *Secretary*, R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.
- Obstetrical Society of Philadelphia.** (1868) *President*, F. Sidney Dunn. *Secretary*, James P. Lewis, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.
- Chicago Gynecological Society.** (1878) *President*, James E. Fitzgerald. *Secretary*, Herbert E. Schmitz, 25 East Washington Ave., Chicago, Ill., Third Friday, From October to June, Hotel Knickerbocker.
- Brooklyn Gynecological Society.** (1890) *President*, John J. Madden. *Secretary*, William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.
- Baltimore Obstetrical and Gynecological Society.** (1929) *President*, Lawrence Wharton. *Secretary-Treasurer*, John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.
- Cincinnati Obstetrical Society.** (1876) *President*, Carroll J. Fairo. *Secretary*, Joseph G. Crotty, 136 West McMillan St., Cincinnati, Ohio. Third Thursday of each month.
- Louisville Obstetrical and Gynecological Society.** *President*, Layman A. Gray. *Secretary*, E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.
- Portland Society of Obstetrics and Gynecology.** *President*, Charles Hunt. *Secretary-Treasurer*, Karl H. Martzloff, 808 Medical Dental Bldg., Portland, Ore. Last Wednesday of each month.
- Pittsburgh Obstetrical and Gynecological Society.** (1934) *President*, James S. Taylor. *Secretary*, Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.
- Obstetrical Society of Boston.** (1861) *President*, George Van S. Smith. *Secretary*, Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.
- New England Obstetrical and Gynecological Society.** (1929) *President*, Roy J. Hefferman, Brookline, Mass. *Secretary*, Fred J. Lynch, 475 Commonwealth Ave., Boston, Mass. Meetings held in May and December.
- Pacific Coast Obstetrical and Gynecological Society.** (1931) *President*, Goodrich C. Schaffer. *Secretary-Treasurer*, William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.
- Washington Gynecological Society.** (1933) *President*, James R. Costello. *Secretary*, Geo. J. Ellis, 1150 Connecticut Ave., N.W., Washington, D. C., Fourth Saturday, October to May.

\*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

The average age of our patients with vulvar cancer was 59 years when they were first seen. This is in close accord with that reported in other studies.<sup>4, 7</sup> It is, in general, a disease of advanced years. In the series of thirty cases which we studied, there were seven patients 70 years of age or over, and eleven patients 65 years or more. As with all cancer groups, there was a wide range in age, our youngest patient being 37 years of age. It is important, therefore, not to allow the general age incidence figures to influence us in the differential diagnosis of the individual case with a vulvar lesion.

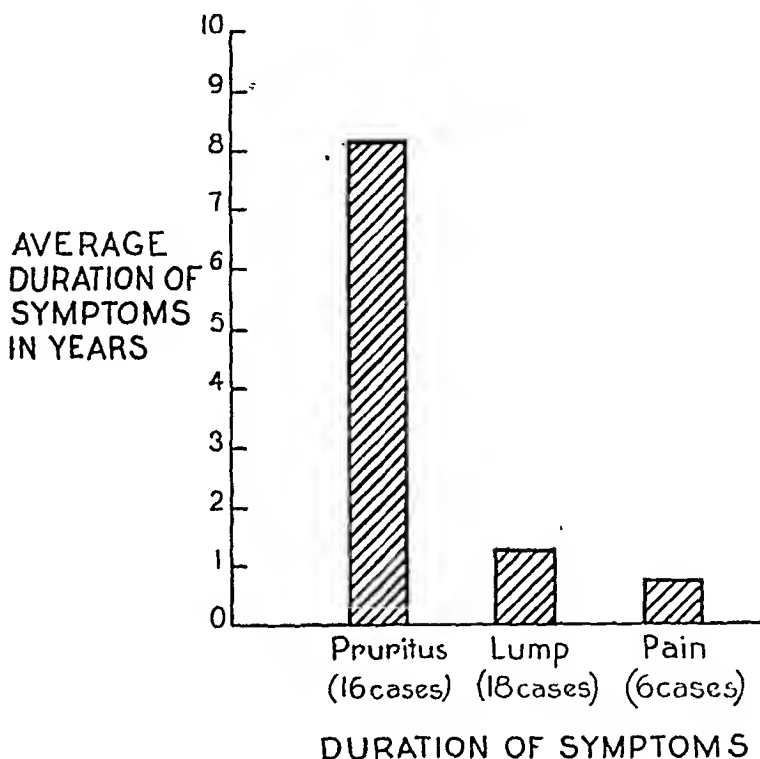


Fig. 1.

The remarkable delay between the onset of symptoms and treatment of the cancer is a phenomenon which everyone has noted in studying this disease.<sup>1, 4, 7, 8</sup> The average delay from the onset of vulvar symptoms to treatment of the cancer in our group was three and three-fourths years. Many of the patients had consulted a doctor much earlier, but he had minimized the condition. Vulvar lesions are not silent as a rule. Important symptoms in our series were pruritus in sixteen cases, a lump in eighteen cases, pain in six cases, and local discharge in two cases. It is interesting to examine the principal symptoms individually in respect to their duration before final treatment. The groups varied strikingly. Fig. 1 graphically illustrates the average duration of the principal symptoms before the cancer treatment. Pruritus was notably the longest with an average of 8.1 years; the symptom of a lump or local growth was present for an average of 1.25 years; the presence of pain was noted for an average of 0.69 years. It would seem probable that this variation is due to several factors: (a) the difference in unpleasantness of the symptom to the patient; (b)

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No. 2

## Original Communications

### PREVENTION AND TREATMENT OF CARCINOMA OF THE VULVA\*

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*(From the Sloane Hospital for Women and the Department of Obstetrics and Gynecology,  
Columbia University)*

CARCINOMA of the vulva is one of the rarer gynecologic lesions. Like carcinoma elsewhere, successful treatment depends very largely upon early diagnosis. An even more important factor is the recognition and treatment of conditions which predispose to the disease.

This study does not deal with a large series of cases and therefore is not statistically important, but it may emphasize certain significant correlations which our experience has suggested. The disease is an uncommon one; it falls into an age group in which life expectancy in general is not long; it is our belief, therefore, that the problem is such as to call for some latitude in the application of the usual standards set up for cancer therapy.

#### Symptoms and Prevention

This aspect of the disease cannot be too frequently stressed, for vulvar conditions which are related to the development of cancer are seen with some frequency. Any irritated or ulcerated lesion which does not yield within a very short time to simple therapy should be subjected to biopsy by free excision. Every leucoplakic area which causes constant itching, necessitating scratching for its relief—with consequent breaking or fissuring—should be excised. This excision may have to include all the vulvar structures. Ointments, hormones, and x-ray therapy have no place in such cases. The direct relationship between leucoplakia of the vulva and cancer has been amply demonstrated by Taussig<sup>3</sup> and others.<sup>6, 18</sup>

\*Read before the Meeting of the New York Obstetrical Society on Jan. 8, 1946.



The group of cases which we studied were treated by various methods, some of which have been little used in recent years, others of which are adaptable only to isolated cases with complicating factors.

Table III illustrates this variety of treatment which has been used:

TABLE III. TREATMENT

PRIMARY TREATMENT	NO. OF CASES	DEAD WITH DISEASE
Complete vulvectomy with bilateral groin dissection	5	1
Above surgery plus radiation	2	1
Complete vulvectomy with unilateral groin dissection	2	0
Above surgery plus radiation	1	0
Complete vulvectomy	2	0
Above surgery plus radiation	1	1
Partial vulvectomy with bilateral groin dissection	1	0
Above surgery plus radiation	0	0
Partial vulvectomy with unilateral groin dissection	0	0
Above surgery plus radiation	1	0
Partial vulvectomy	8	0
Above surgery plus radiation	3	1
Radiation only	4	4

It can be seen that all our treatment groups are small; appraisal of our plan of treatment is more readily obtained from a discussion of our failures than from our successes. An analysis of our fatal cases will be presented, therefore, at a later point.

The treatment employed is primarily surgical. Most of the cases in which radiation was added to the surgical treatment date back a number of years before treatment was well defined. The addition of radiation to one extensive case, which involved the vagina (see below) as well as the vulva, did not appear to add any benefit to the original complete vulvectomy and bilateral groin dissection, for the patient died within one year. Along with most other clinics we have discarded radiation as a primary treatment, except as a palliative. In four extensive cases in which both vagina and vulva were involved when first seen, radiation alone was used as a more or less palliative treatment. None of these survived longer than one and one-half years. We do have one rather unusual patient who came in with a similarly extensive lesion to that described above, and has survived for over five years. She was treated by partial vulvectomy, radium needles locally, and x-ray therapy. She is the only patient in our group with vaginal involvement who survived. Whether or not the interstitial radiation was responsible for this we cannot say.

We have subjected one group of patients to simple partial vulvectomy, and it is important to note that none of these patients died with the disease. It is our opinion that a simple wide excision of this type is the best biopsy method for vulvar lesions, if there is doubt concerning the character of the tumor. This will save a small group of cases—where the malignancy is low grade—from an unnecessarily radical operation. Therapeutically, this method was used in our series for basal cell lesions and other malignancies of very low grade; it was also used as a palliative procedure in several elderly patients with cardiovascular disease, rendering them had operative risks. In our opinion wide local excision is an adequate treatment for basal cell lesions, and for squamous-cell lesions of

the difference in correlation of these symptoms in the lay mind with publicized cancer threats; (c) the difference between the symptoms in their relation to the actual presence of carcinoma; pruritus may often be associated with leucoplakic lesions, while a lump and pain are more strikingly associated with the growth or ulceration of a well-defined tumor.

It would appear from these figures that this group of patients, like all other vulvar carcinoma groups, include many individuals who had lesions which should have brought them to surgical therapy much earlier. Pruritus is a particularly significant symptom in this regard, and its importance cannot be overstressed.

### Treatment and Results

As we have stated previously, the number of our cases, thirty, is not large enough to make this study statistically important. They are presented because we believe from our limited experience that certain deviations from the generally accepted requirements for the surgical removal of a carcinoma are not only permissible but desirable in individual cases.

TABLE I. SURVIVAL AFTER TREATMENT

TOTAL GROUP OF CASES: 30		
TIME (YEARS)	NO. CASES	PERCENTAGE
2	17	56.6
3	15	50.0
5	11	36.6

TABLE II. SURVIVAL AFTER TREATMENT

TOTAL GROUP (INCLUDING ONLY CASES DEFINITELY PRIMARY ON VULVA): 25		
TIME (YEARS)	NO. CASES	PERCENTAGE
2	16	64.0
3	14	56.0
5	10	40.0

The total survivals in our group of cases are presented in Tables I and II. We are submitting the total results for all of our thirty cases, and also correcting these figures in Table II to exclude five cases which appeared in our hospital with a lesion, both in the vagina and on the vulva, of such a distribution that it was impossible to be certain whether or not the lesion was primary on the vulva. We are including two- and three-year survivals in our figures because all of our fatal cases dying with the disease did so before two years had elapsed from the time of treatment. The one patient who died with disease in three years was without doubt suffering from an entirely new and separate carcinoma. Our only other late local recurrence (three years) also appeared to have a new lesion in a leucoplakic area. This impression of early recurrence in cases where treatment fails and the separate identity of most so-called late recurrences is heightened by study of the cases reported in the literature.

Unfortunately, some of our cases have been treated in comparatively recent years. The dropping percentage in the tables represents for the most part this follow-up element rather than increased deaths.

When the groin dissections are completed, the inguinal incisions are joined by a transverse incision across the superior border of the mons veneris. This allows removal of the presymphyseal nodes and lymphatic channels. The block dissection is then continued with excision of all vulvar structures. All tissue is thus removed in one piece. Figs. 2 and 3 illustrate a typical lesion and the extent of the removal.



Fig. 3.—Tissue removed at operation in case illustrated in Fig. 2.

We do not find this one-stage operation ordinarily too shocking if a meticulous technique is rigorously followed, nor do we find wound breakdown a serious problem. While minor wound difficulties have occurred, major ones have been rare.

Study of reported dissections of retroperitoneal nodes does not indicate to us that external iliac and obturator nodes are frequently involved in operable cases.<sup>3, 11</sup> It has been our experience that the state of involvement of these retroperitoneal nodes frequently corresponds with extension of vulvar lesions locally into the vagina. When this occurs, all deep nodes of the pelvis are involved quickly: the hypogastric nodes, the ureteral nodes, and numerous channels in the paravaginal and parametrial tissue. Surgical removal of all this

borderline or potential malignancy, like Bowen's disease.<sup>12</sup> Of course, the usefulness of this operation as a curative measure is limited by the small percentage of cases in which the malignancy is of this low grade character.

In the usual case with carcinoma of the vulva, we prefer complete vulvectomy with bilateral groin dissection. Our group of cases, like that of others, demonstrates the futility of attempting to diagnose involvement of inguinal nodes before operation, for the clinical impression was in error many times in both directions. We do not use the Basset operation.<sup>17, 4, 5, 10, 11</sup> Our technique is a one-stage operation which dissects the superficial inguinofemoral nodes bilaterally, and completely removes the vulvar structures. The groin dissections are done first with incisions paralleling the inferior borders of the inguinal

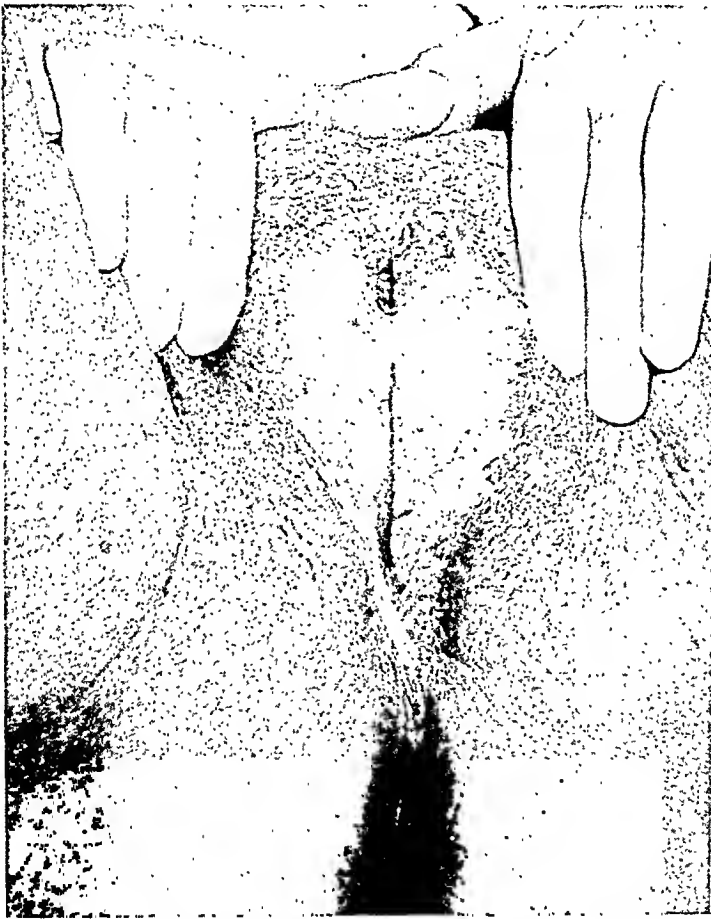


Fig. 2.—Carcinoma in region of clitoris with leucoplakia.

ligaments. Through this incision all the fatty tissue superficial to the inguinal ligament, including the nodes, can be removed; the remainder of the so-called inguinofemoral nodes, which are caudad to the lower border of the inguinal ligament in the superior portion of Scarpa's triangle and over the saphenous opening, are also removed. The external inguinal ring is then incised for several centimeters, and the fatty areolar tissue removed from the inferior portion of the inguinal canal. The internal ring is not incised, nor is the dissection carried to the lowermost portion of Scarpa's triangle; this latter region may be examined by palpation. The retroperitoneal and deep femoral nodes are not dissected.

TABLE IV. FATAL CASES

CASE NO.	SURVIVAL AFTER TREATMENT	SITE OF DISEASE	TREATMENT	CAUSE OF DEATH
1	6 months	Vulva and vagina ? Primary	X-ray	Died with disease
2	1½ years	Vulva and vagina ? Primary	Radium	Died with disease
3	11 months	Vulva and vagina ? Primary	Radium and x-ray	Died with disease
4	1½ years	Vulva and vagina ? Primary	X-ray	Died with disease
5	5 years	Vulva	Partial vulvectomy	Cerebral vascular accident
6	3 years	Vulva	Partial vulvectomy Radium	Died with disease; new lesion
7	24 days	Vulva	Complete vulvectomy; left groin dissection	Pulmonary embolus
8	1 year	Vulva	Complete vulvectomy; bi-lateral groin dissection	Died with disease
9	1 year	Vulva with extension into vagina	Complete vulvectomy; bi-lateral groin dissection and x-ray	Died with disease
10	7 years	Vulva	Complete vulvectomy; bi-lateral groin dissection and x-ray	Pernicious anemia; erysipelas; septicemia
11	1 year	Vulva	Complete vulvectomy; x-ray	Died with disease
12	1½ years	Vulva	Partial vulvectomy; bi-lateral groin dissection	Cardiac disease; diabetes uremia
13	9 years	Vulva	Partial vulvectomy	Carcinoma of cervix

We have seen but one patient with a lesion confined to the vulva and with complete operation performed who died of recurrence. This was Case 8, who was subjected to complete vulvectomy and bilateral groin dissection. The inguinofemoral nodes were negative on pathologic examination. She died with the disease in one year.

### Summary and Conclusions

1. We have reaffirmed the singular importance of prophylaxis in carcinoma of the vulva. Temporizing measures are unjustified in the face of premonitory lesions, whose relation to cancer is evident. The symptom of vulvar pruritus in middle-aged women is a significant one.

2. We have discussed our plan of surgical treatment. We have found the operation of radical vulvectomy with bilateral dissection of the superficial inguinofemoral nodes an efficient one. The use of wide local excision as a biopsy method is proposed, and its therapeutic value in low grade malignancy suggested.

3. The gravity of prognosis with extension of disease into the vagina is notable in our cases. We cannot be as pessimistic as many observers, however, for the general group of vulvar carcinomas. Many of them can be cured.

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tissue is a very extensive undertaking. More than one-third of our cases occurred in patients 65 years of age or over. In this age group Taussig's figures indicate a considerable operative mortality (18 per cent).<sup>4</sup> Since many of our less advanced cases died with cardiovascular or other intercurrent disease and not of cancer, it would appear that our conservatism at the time of operation is justified.

We do not dissect the deep femoral nodes (including Cloquet's node), an omission contrary to the technique of most operators.<sup>4, 5, 11, 16</sup> If operable cases have involvement of this group of nodes as constantly as indicated by some observers, the survival of any of our cases is unexplainable. It is possible that our results were favored by the anatomic distribution in our group. Of 26 cases where the primary site is accurately recorded, there were 19 in which it was situated on the anterior portions of labia, in the vestibule, or in the region of the clitoris. In the other seven cases the perineum, or posterior labial areas, were the sites originally involved.

We do not have a sufficient number of node dissections in our group to have statistically significant data concerning the curability of cases with node involvement. Of eight cases in which bilateral groin dissection was performed, negative nodes were found in four cases, both groins were positive in one case, and one of the groins was positive in three cases. Of the four patients who were subjected to unilateral groin dissection, the nodes were positive in two cases and negative in two cases. Of the six cases with gland metastases we have only two three-year survivals; two patients who survived have not been followed for three years as yet; the two early deaths include one patient who had intravaginal extension when operated upon, and one who died of a non-gynecologic disease.

An analysis of our fatal cases brings out some of the points which have been discussed. The data is presented in Table IV.

Examination of our first four fatal cases reveals the rapid course of the disease when it involves the vagina. It is sometimes impossible to be sure which is the primary site. Various degrees of radiation therapy failed to arrest the disease. Case 9 was a definite vulvar carcinoma which had extended into the vagina and, in spite of treatment which included complete vulvectomy, bilateral groin dissection, and radiation, she died with the disease in one year. It is evident that extension into the vagina makes the prognosis in vulvar cancer extremely grave.

Of the other patients who died with the disease Case 11 was an example of inadequate treatment. The groins were not dissected because this 70-year-old lady was a bad cardiac and poor operative risk. Case 6 was our only patient who died with the disease more than two years after treatment; the lesion from which she died was a new carcinoma rather than a recurrence, for it arose on the other side of the vulva in an entirely new and untreated region. This patient, because of her age, 77 years, was inadequately treated, being subjected only to partial vulvectomy. In three years a leucoplakic area on the opposite labium went on to malignancy—an argument for complete vulvectomy whenever feasible in all cases associated with leucoplakia.

one-third of the patients, first noticed a lump in the vulva, whereas only 23 per cent in each case noticed ulceration or pruritus.

The patients who complained of pain were very few in number; the percentage in this group was 9.3. Pain was usually a later symptom, and the survival rate was not as good. The best survival rate, with regard to the first symptoms was in the group that first noticed a lump, where there was 37.6 for a five-year survival.

It is interesting that of our patients who had had symptoms for over two years, there were 27.9 per cent of five-year survivals. On the contrary, the group showing symptoms for less than six months had only a 9 per cent five-year survival record. This is evidence that the type of tumor rather than the speed of diagnosis and treatment may determine the results.

I was somewhat shocked when I found that only 51 per cent of our group, namely, 44 patients out of 86, came to us untreated from other places. Treatment had been begun either by surgery or radium. Yet our own results in the patients that we received untreated was only 29 per cent, whereas the total was 28 per cent. This would make one feel that other people haven't done much harm in their preliminary unsuccessful efforts.

With respect to the type of treatment, I thoroughly agree with Dr. Watson that the proper treatment is surgery. We have no patient treated with radiation alone who survived five years. We have a certain number of patients treated with irradiation to the groin nodes who survived five years, but they are in the minority. I think that treatment is dissection of the groins and vulvectomy.

The question of whether the complete operation should be done or not depends on several factors. We had not adopted the Basset one-stage procedure as a general procedure in 1936, when the last of these cases was being treated. It was a theory of Dr. Healy at Memorial Hospital that the lymph nodes of the groin should be used as a filter and vulvectomy done, allowing the lymph nodes to recede, if there was a lymphadenitis present, before the dissection was done, so we did not have the breaking down of the inguinal region after operation. That seemed to be the proper procedure. We had much better results with primary healing of the groins when we adopted that procedure.

I have been interested in the question of nationality in connection with carcinoma. Some time ago I studied that question in cancer of the cervix, and found that the Jewish population in the clinic, in general comprising 31 per cent of the total clinic, contributed less than 4 per cent of the cancers of the cervix. Similarly, Jewish women made up only 5 per cent of the cancer of the vulva group. In their prognosis they did very much better than the other groups. In their group four out of five survived for a period of five years, and this is our highest rate in a small number of cases.

Dr. Pollock has reviewed a larger series of Memorial Hospital cases, including my figures and those of the additional ten years through 1945, which will be presented by him.

DR. ROBERT S. POLLOCK (by invitation).—The following statistics are in the nature of a preliminary report. At the present time we are studying 244 cases of cancer of the vulva seen at Memorial Hospital from 1926 through 1945. These cases are being studied from the standpoint of symptomatology and location of the lesion in order to gather general knowledge about the process.

There are 162 recorded cases seen from 1926 through 1940 on which we are reporting five-year "cure" rates. Of this figure, 16 cases were deleted because they were not histologically proved, thus giving us a total of 146 cases. These have been divided into two groups: primary and secondary. The primary cases include those that have come to the hospital without any previous treatment of any kind. The secondary group includes those patients who have had some form of treatment, either at another institution or by an outside physician. This treatment would include x-ray, radium, or surgery.

We have 100 primary cases and 46 secondary cases. The "absolute cure" rate, that is, those cases without evidence of cancer five years after the first treatment, is 26.00 per cent for the primary group and 26.08 per cent for the secondary group.

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### Discussion

DR. S. B. GUSBERG.—In our group of 30 cases, 24 were squamous cell, three basal cell, two melanomas, and one an adenocarcinoma arising from a sweat gland. During this same period our records show six cases of Bowen's disease of the vulva which were treated by excision.

We were attracted to study this small group of cases because of the fact that this carcinoma appeared to be one with a definite precursor which was seen with a fair degree of frequency, namely, leucoplakia of the vulva. This fact appeared to be definitely established in the literature, yet many of our patients were followed for a long time by their physicians and given an amazing array of treatments before they came to their ultimate definitive excision. It appeared to us, therefore, that the significance of vulvar lesions should be stressed, in spite of the fact that carcinoma was rather infrequent, because of the opportunity to remove tissue which might very definitely develop cancer.

DR. FRANK R. SMITH.—Before the war I had prepared a study of carcinoma of the vulva, not for the purpose of presenting any statistics, but with the idea of finding factors in the prognosis of this condition. At that time there were records of 119 patients with carcinoma of the vulva at Memorial Hospital. I was able to cull from the records 86 patients treated at Memorial Hospital up to the year 1936, so in 1941 we had five-year records of these patients. Of that group, our total five-year figure was only 28 per cent. After ten years the survival rate was 14.0 per cent, whereas after fifteen years, it was only 5 per cent. So that, of the patients who survived five years and seemed free of disease, at least 50 per cent of them were going to show a recurrence of the disease after ten years or nonsurvival.

The average age of our cases was 60 years, while Dr. Watson's was 59 years. Forty-one per cent of our group were in the decade from 60 to 70 years. There were 33 per cent of five-year survivals without disease in that particular age group. There were four patients between 25 and 35 years of age. All of the young patients that I have seen were women in whom the carcinoma was superimposed on a skin lesion, such as psoriasis, eczema, or lymphogranuloma. They responded to treatment, i.e., surgery, much more readily than the older patients.

As regards the type and location of the lesion, our results were not good where the lesion was situated around the clitoris. Strangely enough, 46.5 per cent of our patients had the lesion in the left vulva, whereas only 20.9 per cent had it in the right vulva. In about 16 per cent the lesion was around the clitoris. Those who had the lesion on the left vulva had the highest rate of five-year "cure," 32.5 per cent, as compared to 22.2 per cent and 21.4 per cent for the other two locations.

As regards the first symptom noticed, I have always considered leucoplakia and pruritus vulvae as the two cardinal primary ones. Yet in our group, over 31.3 per cent, or nearly



In the entire series of 17 cases, four are living five years or over, an incidence of 23.5 per cent.

I found that with radium the patients suffered great pain and sloughing, so we abandoned it. We feel that in marked cases of leucoplakia or kraurosis, vulvectomy should be done as a prophylactic measure.

Taussig's work is outstanding and his results are most conclusive. In 1940 he presented a paper in which he reported the results in 155 cases, and stated that radium in his hands was also disappointing and that he had abandoned its use. With vulvectomy and the Basset procedure, he expects survival in three out of five cases for a period of five years, or 58.5 per cent, even though two of the five show lymph gland metastasis.

In 1941 a very exhaustive paper was presented by Beven of Stockholm, in which a very thorough statistical study was made of a series of 177 cases in which there was a five-year cure of 36.7 per cent. They used electrocoagulation for removal of the vulvar growth, and then teluradium afterward. If there were any glands present, they did a block dissection. Their postoperative mortality was 8.5 per cent.

I think that today everyone is in agreement that vulvectomy, the classical procedure, thoroughly done, gives the best chance for a five-year cure.

The "determinate group" total is 132. This figure is arrived at after subtracting 14 cases from the 146 cases studied. These 14 cases represent eight who died of other causes and six who were lost track of at a time when they showed no evidence of cancer. There are 90 primary cases and 42 secondary cases in the determinate group, giving a determinate "cure" rate of 28.88 per cent for the primary, and 28.57 per cent for the secondary group.

There is one very interesting inference which may be drawn from the figures of our absolute "cure" rate. The percentages of both the primary and secondary groups are practically identical, and therefore it would seem that there are apparently two types of cancers of the vulva, one which can be cured despite loss of time and inadequate treatment, and another which is recalcitrant to treatment despite the application of all methods of therapy.

DR. MORTIMER D. SPEISER.—During the last ten years we have seen 29 cases of carcinoma of the vulva at Bellevue Hospital. Twenty-six of these were of the squamous-cell variety, and three adenocarcinomas. In the latter Group 2 originated from the Bartholin glands, and in one the origin was not definitely determined.

The primary cases of carcinoma of the vulva numbered 24; of these 10 were inoperable, and 14 were amenable to some type of surgical therapy. The treatment varied. Many cases were subjected to a radical vulvectomy with dissection of the inguinal nodes, while in other cases a radical vulvectomy was followed at a later date, after a week or two, by extensive inguinal node resections employing the Basset technique. Fifty per cent of our cases operated upon either died or showed evidences of recurrences, while the other 50 per cent are alive and well. Further scrutiny of this latter group reveals the fact that only two of these cases have gone for more than five years without recurrences. One patient has now been well for four years, and there are four patients who have been observed for one year or less since their operation. From the standpoint of a five-year salvage rate, there were only two cases out of 24, an incidence of 8.3 per cent, which is very much lower than the results obtained by Dr. Watson. I believe that in our patients the disease is far more extensive at the time of admission to the hospital, and for that reason fully half of our patients were beyond the possibility of any operative intervention. In these cases there was considerable involvement of the vagina, perineum, and perirectal tissues. In those cases in which surgery was undertaken, I believe that the disease again was well advanced as the result of neglect on the part of the patient prior to visiting a doctor. We were, therefore, dealing with a group of patients in whom we expected poor results with any method of therapy. The same condition exists in our cases with carcinoma of the cervix.

DR. GEORGE G. WARD.—In looking up the vulva cancer cases at the Woman's Hospital, I found that in 28,855 gynecologic discharges in the past fifteen years, there were seventeen cases. Of the eleven ward patients four are alive and seven dead. Of the six private cases one is dead, three are alive, and we have lost track of two.

Of the seven living cases, one is living 15 years, one 11 years, one seven years, one five years, and three one year.

We used radium alone in the early cases, but have since abandoned it. Of the cases in which radium alone was used, four in all, one is alive after fifteen years, the others having succumbed. We used radium with vulvectomy in one case, and that patient is still living after eleven years.

There were five cases in which vulvectomy alone was done. In that group two patients were alive after one year, and the other three were dead after five years.

We now do the complete vulvectomy operation in every case and follow it with the Basset procedure. We do not do the two procedures in the same sitting. In doing the Basset procedure we follow Dr. Taussig's well worked-out technique, which is very extensive and which makes a point of getting Cloquet's gland underneath the inguinal ligament, at the femoral ring. There were seven cases in which we did vulvectomy and the Basset procedure, and of that group three are dead and the other four are living, two for one year, one for seven years, and one for eleven years.

TABLE I. ANALYSIS OF 66 CASES OF ASPIRATION

Prolonged labor,	30 hours or over	9	14%
Type of delivery,	Normal spontaneous	29	44%
	Cesarean section	14	21%
	Operative other	23	35%
Anesthesia,	Gas, oxygen, ether	66	100%
Aspiration,	Recorded at delivery	45	68%
	solid	5	
	liquid	40	
	Subsequently diagnosed	21	32%
	Obstructive reaction	5	8%
	suffocation	3	
	massive collapse	2	
	Asthmatic-like reaction	61	92%
Cyanosis,	Recorded	55	83%
Tachycardia,	Pulse over 110 per minute	66	100%
Dyspnea,	Respirations over 30 per minute	66	100%
Chest pathology,	Diffuse	15	23%
	Right only	51	77%
	Left only	0	0%
Morbidity,	Febrile	20	30%
	chest	8	
	pneumonia	6	
	abscess	2	
	other	12	
Chemotherapy,	Sulfonamides	14	21%
	Penicillin	3	5%
	Both	2	3%
Deaths,	Immediate	2	3%
	Later	0	0%



Fig. 1.—Massive collapse of right lung following obstruction by solid, undigested food. Note the mediastinal shift and homogeneous density over the collapsed area.

Obstructive reactions occurred in the five patients that aspirated solid material. Three of these had complete obstruction; two died of suffocation on the delivery table, whereas the third recovered after coughing up a large piece of meat. Two of the five patients had incomplete obstruction with massive atelectasis, and both recovered after coughing up the obstructing material. These patients exhibited the classical picture of massive collapse with cyanosis, tachycardia, dyspnea, evidence of mediastinal shift, and consolidation. Fig. 1 shows the typical chest plate in such a case. There is mediastinal shift and a homogeneous density over the collapsed area on the right side.

# THE ASPIRATION OF STOMACH CONTENTS INTO THE LUNGS DURING OBSTETRIC ANESTHESIA\*

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IN MOST texts on pulmonary complications, aspiration of stomach contents into the lungs during general anesthesia is considered under the heading of postanesthetic pneumonia. Aspiration of infected material is said to produce atelectasis, pneumonia, and lung abscess.

A survey of New York Lying-In Hospital records of patients that aspirated gastric contents during obstetric anesthesia revealed the following different diagnoses: suffocation, massive atelectasis, partial atelectasis, disc atelectasis, pulmonary infarct, aspiration pneumonia, bronchopneumonia, lobar pneumonia, virus pneumonia, atypical pneumonia, tuberculous pneumonia, pulmonary tuberculosis, fungus infection, pulmonary metastasis, drowned lung, cardiac failure, pulmonary edema, and paroxysmal tachycardia. Obviously, a better understanding of this condition is wanting.

## Present Study

There have been sixty-six instances of aspiration of stomach contents into the lungs in 44,016 pregnancies at the Lying-In Hospital from 1932 to 1945. The incidence of this complication is 0.15 per cent.

An analysis of the cases is presented and followed by experimental work to clarify the pathology of aspiration, and thereby gain insight into its diagnosis, prevention, and treatment.

## Analysis of Cases

The significant data in the 66 cases are summarized in Table I.

The incidence of prolonged labor was somewhat higher than that of the total clinic population, which is 10 per cent.

## Obstetric Reactions

Slightly more than half of the cases had operative intervention requiring relatively longer administration and greater depth of anesthesia than those delivered spontaneously. A mixture of gas, oxygen, and ether was employed in all instances.

## Aspiration

Aspiration was recorded as having definitely occurred in the delivery room in 68 per cent. In 32 per cent this complication went unrecognized until later. The character of the aspirated material in the 45 recorded cases was liquid in 40 and solid in five.

\*Read at a meeting of the New York Obstetrical Society, Dec. 11, 1945.

and rhonchi. High pulse and respiratory rates were common, often reaching values of 160 and 40 respectively. Evidence of cardiac failure frequently appeared, and occasionally culminated in pulmonary edema.

The patients were critically ill during the acute episode, but there was gradual stabilization within twenty-four to thirty-six hours, and recovery was usually complete with an afebrile and uncomplicated course.

Early x-rays revealed irregular, soft, mottled densities in the involved areas, but no mediastinal shift. Subsequent films usually showed complete clearing within seven to ten days. These features are illustrated in Figs. 2, 3, 4, and 5.

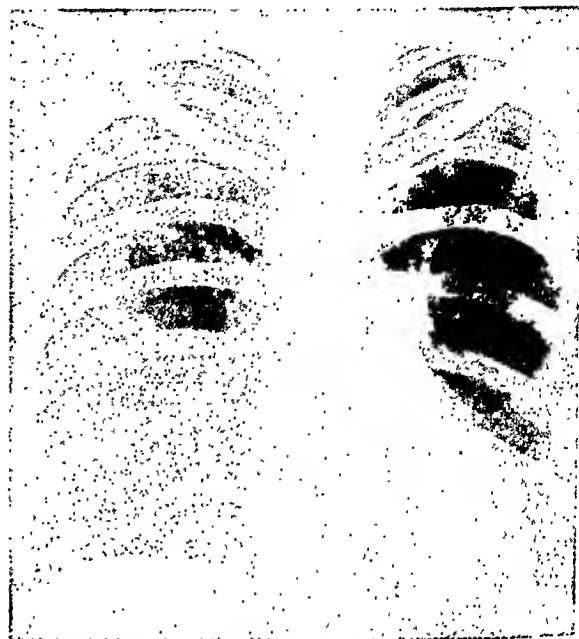
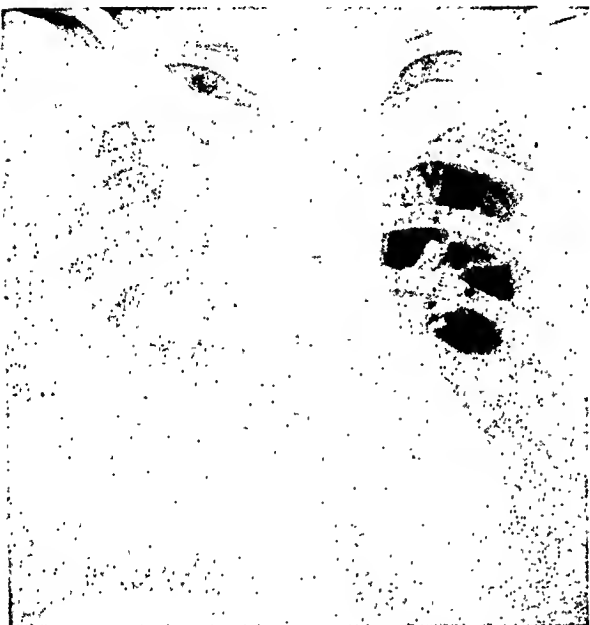


Fig. 4.—Another case after the aspiration of liquid gastric contents.

Fig. 5.—The same patient as in Fig. 4, seven days later.

### Cyanosis, Tachycardia, Dyspnea

Cyanosis, tachycardia, and dyspnea occurred in most cases, regardless of the type of aspiration.

### Chest Pathology

The right lung was most commonly involved in both types of aspiration. Massive aspiration, however, readily involved both lungs.

### Morbidity and Chemotherapy

The morbid group includes any patient with elevation of oral temperature to 38° C. (100.4° F.) during any two twenty-four-hour periods postpartum, exclusive of the first twenty-four hours following delivery. Thirty per cent of all cases were morbid, but less than half the morbidity was attributable to chest pathology. Many cases occurred before the use of sulfonamides and penicillin, so that relatively few received this type of chemotherapy, yet only six patients developed pneumonia. Two of the pneumonia cases followed the obstructive type of reaction, and four followed the asthmatic type. One of each of these groups went on to develop a lung abscess. Fortunately all these patients recovered. Infection must be regarded as a relatively infrequent but serious secondary complication.

### Asthmatic-like Reactions

A very different type of reaction was observed in the 40 patients that aspirated liquid material. For lack of any existing description, this type of reaction may best be likened to an acute asthmatic attack.

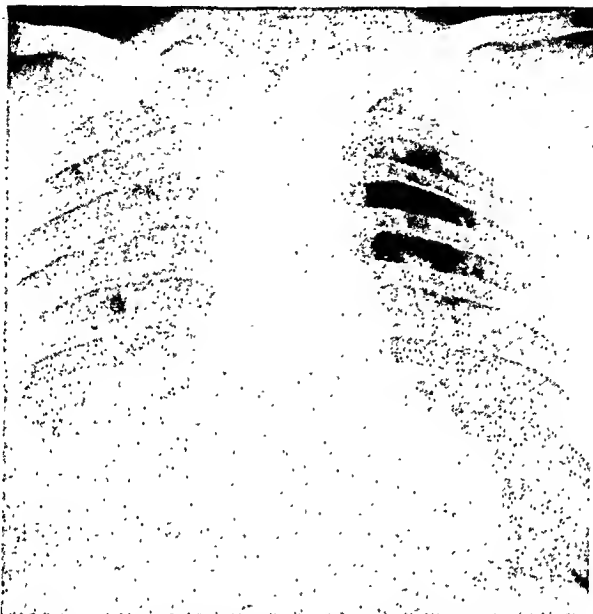


Fig. 2.—Scattered soft, mottled, confluent densities seen after aspiration of liquid gastric contents. Note the absence of any mediastinal shift.

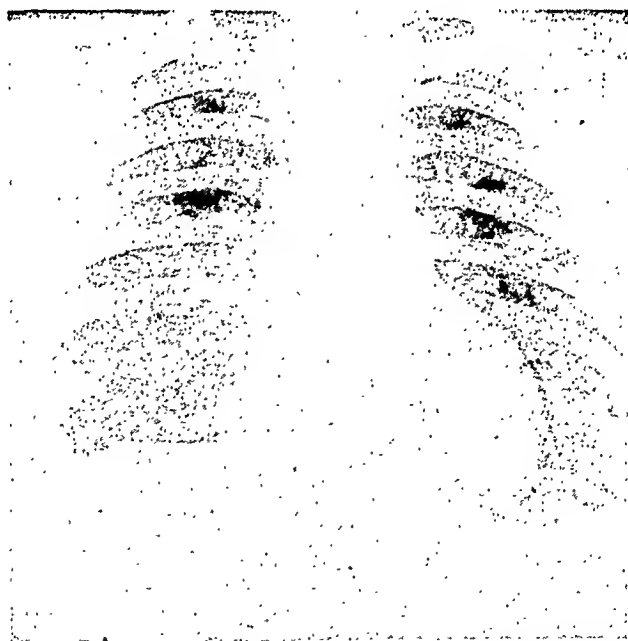


Fig. 3.—The same patient as in Fig. 2, ten days later.

Apparently liquid gastric contents were aspirated into the lungs, while the laryngeal reflexes were abolished during general anesthesia. The actual aspiration often escaped recognition. Cyanosis, tachycardia, and dyspnea developed as in the obstructive cases, but there was no massive atelectasis or mediastinal shift. Auscultation over the involved areas revealed numerous wheezes, râles,

appearance of massive atelectasis. Practically all crepitation is gone, but otherwise the gross picture is not remarkable. There is no free fluid in the pleural or pericardial cavities. The heart and abdominal viscera are normal. The typical microscopic picture of atelectasis is seen in Fig. 8.

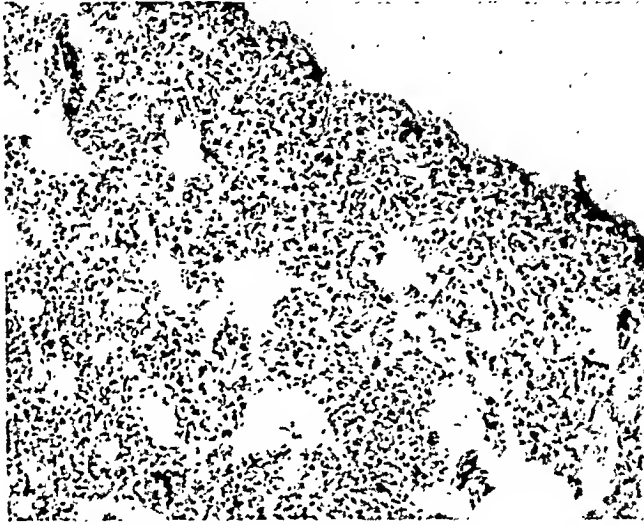


Fig. 8.—Section of a rabbit lung showing massive atelectasis.

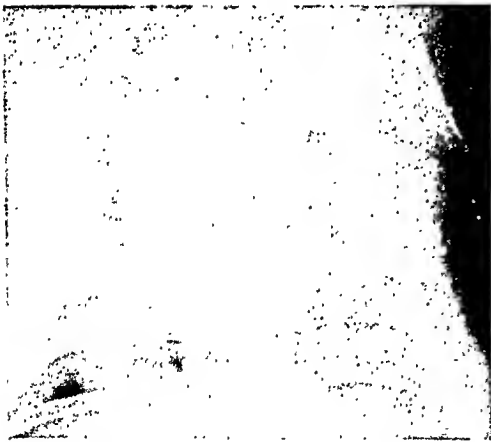


Fig. 9.—Chest film of a rabbit after aspiration of 20 c.c. of tenth normal hydrochloric acid. Note the soft, mottled, confluent densities and absence of any mediastinal shift.

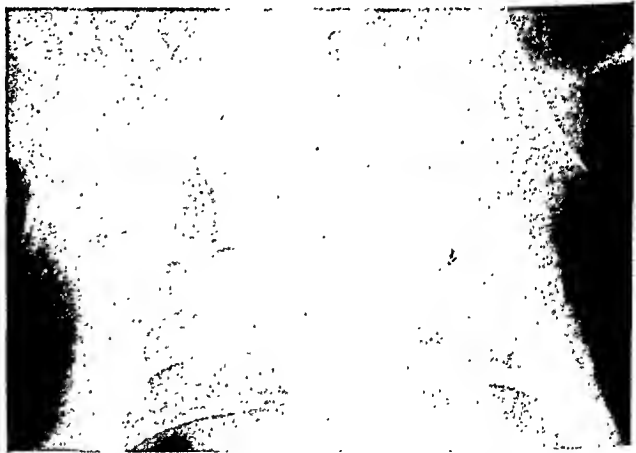


Fig. 10.—Chest film of a rabbit after aspiration of 20 c.c. of unneutralized liquid gastric contents. Note the similarity to Fig. 9.

Following aspiration of liquid containing hydrochloric acid (tenth normal hydrochloric acid or unneutralized liquid vomitus) the animals develop a syndrome similar in many respects to that observed in the human following liquid aspiration. Cyanosis and labored respirations develop immediately, but death often ensues within minutes to hours, with a pink froth exuding from the respiratory passages in the terminal stages. X-rays reveal irregular, soft, mottled shadows without mediastinal shift. Fig. 9 shows the picture after aspiration of 20 c.c. of tenth normal hydrochloric acid, and Fig. 10 shows practically identical findings after aspiration of 20 c.c. of unneutralized liquid vomitus. The gross pathologic picture may be described as follows: The trachea is injected and filled with pink frothy material. The pleural cavities contain a

### Mortality

The two deaths in the series were due to suffocation from complete obstruction by solid undigested food. Both patients had recently ingested a full meal; one eight hours previously, the other six hours previously. Autopsy obtained in the latter case revealed complete obstruction of the major respiratory passages by solid food particles.

None of the cases in the series suffered from pulmonary tuberculosis, primary organic heart disease, concurrent respiratory infection, or malignancy.

### Experimental

A series of animal experiments were undertaken to determine the pathology of these two different aspiration syndromes. Anyone who has aspirated the slightest amount of fluid during a vomiting seizure will remember the intense irritation produced. It was thought pertinent to evaluate the role of hydrochloric acid.

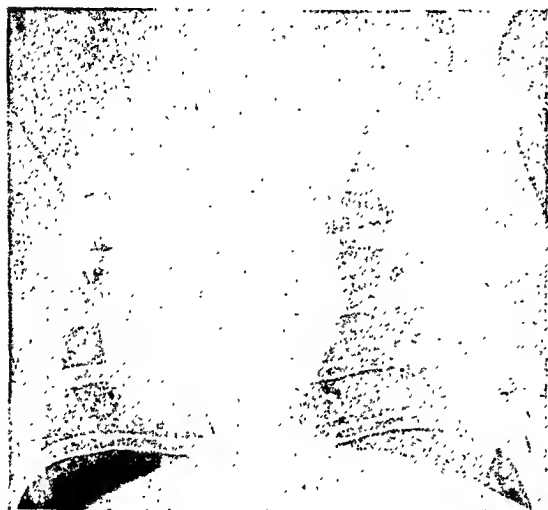


Fig. 6.—Chest film of normal rabbit.

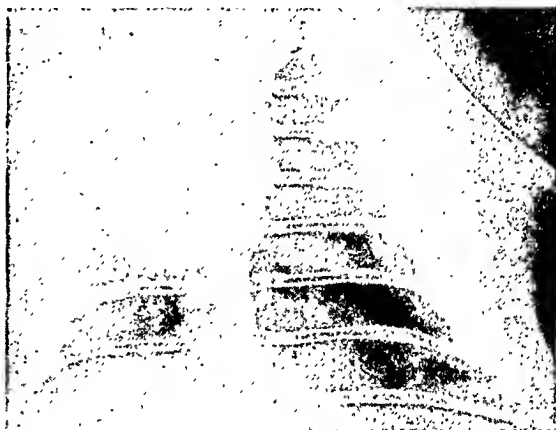


Fig. 7.—Chest film of a rabbit after obstruction by solid undigested food. Note the mediastinal shift and homogeneous density over the collapsed area.

Various materials were introduced into the lungs of adult rabbits weighing between 5 and 6 kilograms. In some instances the material was introduced using a laryngoscope during sodium pentothal anesthesia, while in others the material was introduced directly into the trachea after preliminary tracheotomy.

The following substances were used: distilled water, normal saline, tenth normal hydrochloric acid, liquid vomitus, neutralized liquid vomitus, vomitus containing solid undigested food, and neutralized vomitus containing solid undigested food. All vomitus was obtained from parturient patients, none of whom suffered from achlorhydria. Such material was used in its acid state unless subsequently modified to a neutral pH, as previously indicated.

The experimental results may be summarized as follows. After aspiration of solid undigested food the picture is invariably that of obstruction as observed in the human. This is true regardless of whether acid or neutral material is used. Complete obstruction causes suffocation. Incomplete obstruction produces massive atelectasis. The chest film of a normal rabbit is shown in Fig. 6. Fig. 7 shows the picture with massive collapse following incomplete obstruction. Note the homogeneous density and mediastinal shift. Animals relieved of obstruction recover completely. The collapsed lung shows the typical



11 shows the lungs after aspiration of 20 c.c. of tenth normal hydrochloric acid, and Fig. 12 shows a similar picture after aspiration of 20 c.c. of unneutralized liquid vomitus. On cut section the lungs exude a pink gelatinous material. The heart is dilated and shows small subpericardial hemorrhages. There is congestion of all the abdominal viscera.



Fig. 13.—Section of rabbit lungs after aspiration of 20 c.c. of tenth normal hydrochloric acid. Note the bronchiolar pattern with necrotic epithelium partly sloughed into the lumen, and the peribronchiolar congestion.



Fig. 14.—Section of rabbit lungs after aspiration of 20 c.c. of unneutralized liquid gastric contents. Note the character of the alveolar walls with pyknotic nuclei and the exudate within the alveoli.

The microscopic picture is also the same after aspiration of equal amounts of tenth normal hydrochloric acid or unneutralized liquid vomitus. The trachea and larger bronchi are congested, but the epithelium is intact. A wavy bronchiolar pattern is noted, indicative of muscular spasm. There is peribronchiolar hemorrhage and exudate with areas of surrounding emphysema. In places the bronchiolar epithelium is necrotic and sloughed into the lumen. The alveolar walls are hyaline with absent or pyknotic nuclei. Perivascular edema is marked. There is congestion and edema throughout. Figs. 13 and 14 demonstrate the above features.

serosanguineous fluid. The visceral pleura is smooth with large subpleural hemorrhages, imparting a variegated color to the lungs, ranging from normal pink through all the shades of red to a rich dark purple. The darker areas are doughy in contrast to the pink areas which retain normal crepitation. The lungs are heavier than normal. Scatter emphysematous blebs are present. Fig.

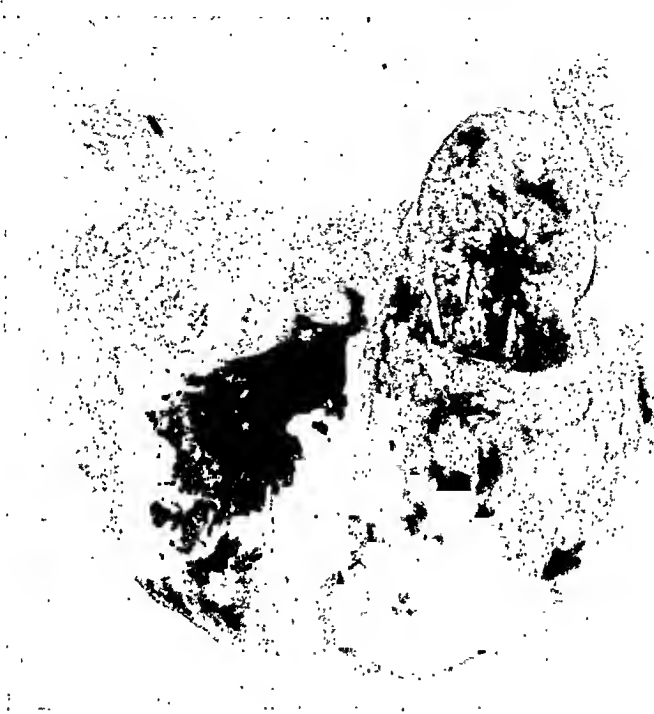


Fig. 11.—Lungs of a rabbit after aspiration of 20 c.c. of tenth normal hydrochloric acid. The darker areas are hemorrhagic and doughy.

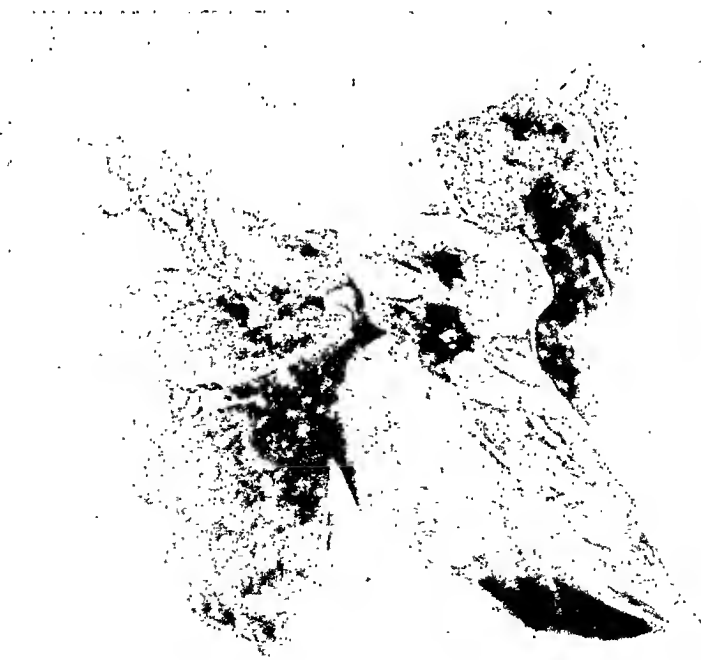


Fig. 12.—Lungs of a rabbit after aspiration of 20 c.c. of unneutralized liquid gastric contents. Note the similarity to Fig. 11.

and Fig. 18 shows the lungs after aspiration of 20 c.c. of neutralized liquid vomitus. The cut surface of the lungs is normal. The heart and abdominal viscera are unremarkable.

The microscopic picture is not remarkable except for small patches of atelectasis and emphysema. There are no bronchiolar changes. Hemorrhage, congestion, edema, and exudate are absent. Fig. 19 shows a section from the lungs after aspiration of 20 c.c. of normal saline, and Fig. 20 shows a section following aspiration of 20 c.c. of neutralized liquid vomitus.



Fig. 18.—Lungs of a rabbit after aspiration of 20 c.c. of neutralized liquid gastric contents. Essentially the same as Fig. 17.

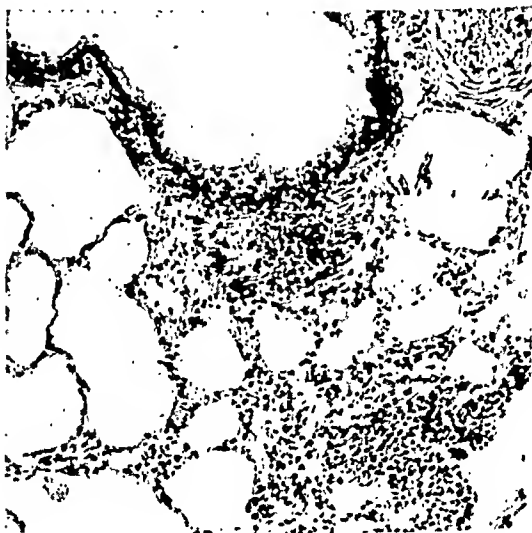
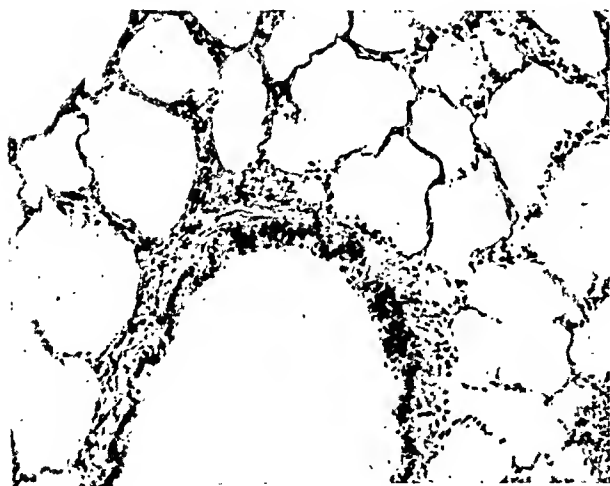


Fig. 19.—Section of rabbit lungs after aspiration of 20 c.c. of normal saline. There is slight emphysema, but otherwise the section is unremarkable.

Fig. 20.—Section of rabbit lungs after aspiration of 20 c.c. of neutralized liquid gastric contents. There is a small area of atelectasis.

Following aspiration of neutral liquid (distilled water, normal saline, or neutralized liquid vomitus) in equal quantities to the preceding series of acid experiments, the animals go through a brief phase of labored respirations and cyanosis, but within a few hours they are apparently back to normal, able to carry on rabbit activities uninhibited. There are no significant x-ray changes. Fig. 15 shows the chest film after aspiration of 20 c.c. of normal saline and Fig.

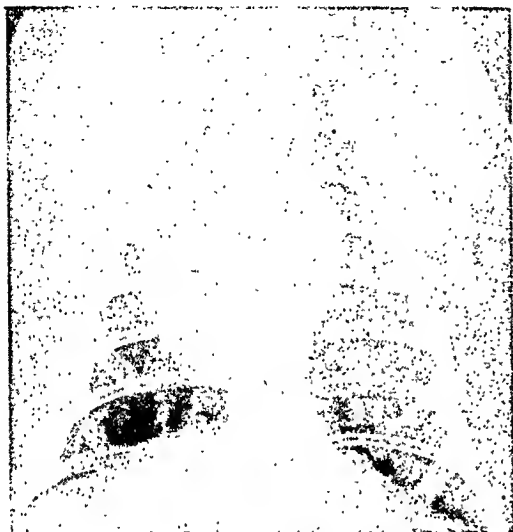


Fig. 15.—Chest film of a rabbit after aspiration of 20 c.c. of normal saline. There are no significant changes.

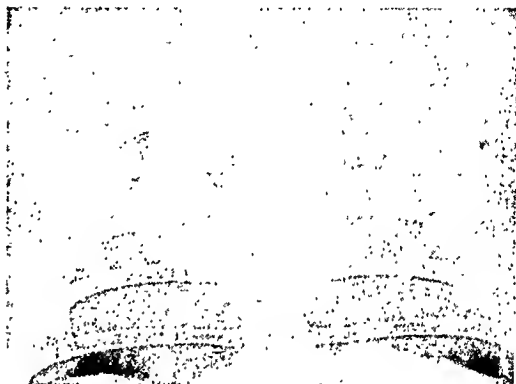


Fig. 16.—Chest film of a rabbit after aspiration of 20 c.c. of neutralized liquid gastric contents. There are no significant changes.

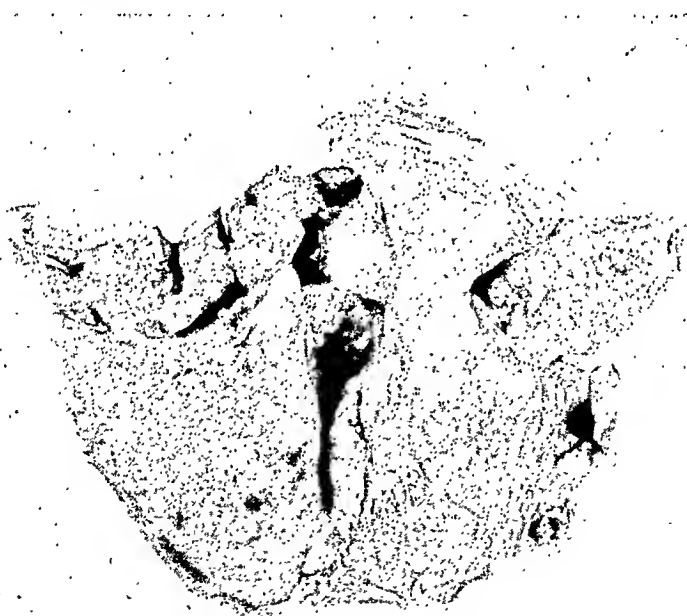


Fig. 17.—Lungs of a rabbit after aspiration of 20 c.c. of normal saline. Except for minute hemorrhagic areas, the lungs are not remarkable.

16 shows the film after aspiration of 20 c.c. of neutralized liquid vomitus. The gross pathologic changes are minimal. The trachea and larger bronchi are normal. There is no free fluid in the pleural or pericardial cavities. The lungs show minute scattered areas of atelectasis, but for the most part are crepitant throughout. Fig. 17 shows the lungs after aspiration of 20 c.c. of normal saline,

tion of tenth normal hydrochloric acid and unneutralized liquid gastric contents are similar to those following gassing with chlorine and phosgene, but there is less necrosis after aspiration, probably because of smaller concentration of the irritant.

Therapy in this type of aspiration should be directed against the bronchiolar spasm and cardiac embarrassment. Oxygen, atropine, adrenaline, and aminophylline will accomplish these objectives. Should evidence of cardiac failure develop, rapid intravenous digitalization is indicated. The circulatory burden may be further relieved by the application of tourniquets to the extremities to produce the effect of a bloodless phlebotomy.

The dramatic relief reported<sup>2, 3</sup> in the treatment of acute asthma by stellate ganglion block suggests that this procedure may be of value. The fundamental neurophysiology of stellate ganglion block is not clear, but the technique of performing the block is relatively simple. So far it has not been tried in the treatment of this type of aspiration.

The bronchoscope would appear to be of little value in this condition, for the pathologic process is beyond reach, and endoscopy may only increase the existent spasm and dangers of secondary infection.

The majority of patients have an afebrile recovery with complete clearing of the chest in seven to ten days. The pathologic process is primarily irritative and not infectious, but sulfonamides and penicillin may be of value in preventing secondary infection due to concurrent aspiration of nasopharyngeal flora.

It is conceivable that both solid and liquid aspiration may occur simultaneously, in which instance both the obstructive and asthmatic pictures would be found. In the present series this situation has not been encountered. Presumably the presence of any solid material so alters the consistency of the gastric contents that little material reaches the bronchioles.

It is important to appreciate that both types of aspiration are preventable. The delayed emptying time of the stomach during labor has already been discussed. The necessity of feeding the parturient has been overemphasized. Misinformed friends and relatives often urge the patient to ingest a heavy meal early in labor before going to the hospital. This food is supposed to provide strength for parturition. It is obviously dangerous to give any solid food during labor and it would be judicious to explain this to the patient during the prenatal course.

The dangers of fluid aspiration have been overlooked, for it is common hospital practice to urge water, tea, and fruit juices throughout the first stage of labor. It has already been pointed out that copious amounts of liquid may be retained in the stomach and that aspiration of liquid occurs much more frequently than aspiration of solid material.

It is common surgical practice to withhold all feeding for twelve hours or longer before any elective operation. This procedure plus the delayed emptying time of the stomach during labor probably account for aspiration being less of a surgical than an obstetric hazard. While it is true that the parturient expends considerably greater energy than the preoperative patient, it is unlikely that any serious harm would result from withholding all oral feeding for the

## Discussion

The gastric emptying time is often prolonged during labor. This applies to liquid as well as solid stomach contents. At delivery it is not uncommon for a patient to vomit food ingested twenty-four to forty-eight hours previously. As much as a liter of clear to dark green fluid has been recovered from a single patient.

Aspiration of vomitus may occur while the laryngeal reflexes are abolished during general anesthesia. Bronchial configuration favors right-sided aspiration, but massive aspiration readily involves both lung fields. Liquid material is more commonly aspirated than solid. The consistency and dimensions of solid food probably interfere with its aspiration.

This study reveals that two entirely different syndromes may follow aspiration. Aspiration of solid food usually produces the well-known picture of laryngeal or bronchial obstruction. Complete obstruction produces suffocation. Incomplete obstruction produces massive atelectasis with the classical picture of cyanosis, tachycardia, dyspnea, mediastinal shift, and signs of consolidation over the collapsed area. X-rays reveal a homogeneous density in the affected area and varying degrees of mediastinal shift. The pathology of atelectasis is well described in all textbooks dealing with the subject.

Obstruction should be promptly relieved either indirectly by external stimulation with encouragement of coughing, or directly with the aid of suction and endoscopic removal.

The value of sulfonamides and penicillin for this type of aspiration is questionable. Although the process is not primarily infectious, the seriousness of secondary pneumonia and lung abscess may make such chemotherapy worthwhile as a prophylactic measure.

Aspiration of liquid material produces an asthmatic-like syndrome with distinct clinical, roentgenologic, and pathologic features. Apparently this syndrome has escaped recognition, for to the author's knowledge it has not been previously described. There is cyanosis, tachycardia, and dyspnea, but no mediastinal shift or massive atelectasis. Wheezes, râles, and ronchi are heard over the affected portions of the lungs.

X-rays reveal irregular, soft, mottled densities without mediastinal shift. The picture has been misinterpreted as bronchopneumonia, tuberculosis, fungus infection, and even metastasis.

Progressive cardiac embarrassment and pulmonary edema may supervene, regardless of the previous normal condition of the heart. Here the diagnosis has been confused with primary cardiac failure.

The animal experiments indicate that hydrochloric acid is responsible for the changes described. The acid produces a bronchiolar spasm and a peri-bronchiolar congestive and exudative reaction interfering with normal intrapulmonary circulation to the extent that cardiac failure may develop.

The irritative action of hydrochloric acid on the respiratory tract has been previously studied by Winternitz,<sup>1</sup> specifically in reference to the action of chlorine and phosgene in war gas poisoning, but any relation to the pathology of aspiration appears to have been overlooked. The changes following aspira-

4. Liquid material is more frequently aspirated than solid.
5. Aspiration of solid material usually produces the classical picture of laryngeal or bronchial obstruction.
6. Aspiration of liquid produces an apparently hitherto unrecognized asthmatic-like syndrome with distinct clinical, roentgenologic, and pathologic features. This syndrome is due to the irritative action of gastric hydrochloric acid, which produces bronchiolar spasm and a peribronchiolar exudative and congestive reaction.
7. Aspiration of stomach contents into the lungs is preventable. The dangers of this complication as an obstetric hazard may be avoided by: (a) withholding oral feeding during labor and substituting parenteral administration where necessary; (b) wider use of local anesthesia where indicated and feasible; (c) alkalization of, and emptying the stomach contents prior to the administration of a general anesthetic; (d) competent administration of general anesthesia with full appreciation of the dangers of aspiration during induction and recovery; (e) adequate delivery-room equipment, including transparent anesthetic masks, tiltable delivery table, suction, laryngoscope, and bronchoscope; and (f) differential diagnosis between the two syndromes described, and prompt institution of suitable therapy.

NOTE.—The factors used in the animal x-ray experiments were: 50 kilovolt peak, 36 inches, 3 seconds, 40 milliamperes, using a cassette and Bucky diaphragm.

The author wishes to thank the members of the Lying-In staff for permission to use the private cases included in this study. Acknowledgment of technical assistance in the animal x-ray work is expressed to Miss Mildred Powlitis.

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### Discussion

DR. PALUEL J. FLAGG (by invitation).—I would like to present several observations. It seems to me that these accidents may be divided into the acute emergency, the asphyxial accident that occurs on the operating table, and the postasphyxial problem presented by the aftercare. It seems strange to me that there is no anesthetist on this program, as it largely is an anesthetic problem. It confirms an impression I have had for a long time, that we need a pneumatologic service in our hospitals, and that means a group who will care for the administration of gases, for the control of open anesthesia and, of course, we include local and basal anesthesia and other methods of general, as well as the use of gases for resuscitation, and the use of gases for inhalation throughout all the postasphyxial stage.

The pathology that has been described here seems to line up very closely with the pathology we meet with in anoxia. The studies as to the effect of hydrochloric acid are rather new, but the other phenomena that were described are quite usual in anoxic anoxia and obstructive asphyxia.

I desire to present a case which bears out the need of the triple service which I have referred to.

The operation was a cesarean section, done Jan. 9, 1940. No premedication. Gas-oxygen-ether anesthesia was used. Induction was smooth—relaxation early; pronounced salivation; high oxygen concentration maintained to the delivery of the infant, which was somewhat dusky in appearance, but breathed spontaneously.

average duration of labor. Should fluid and caloric balance be disturbed in the event of prolonged labor, parenteral therapy is available.

Even if oral feedings were withheld during labor, it is possible that the stomach might still elaborate and retain sufficient hydrochloric acid to produce a serious aspiration hazard. This danger could be readily avoided by emptying the stomach prior to the administration of a general anesthesia. The time-honored finger in the throat method is always available, but the oral administration of a warm alkaline solution would in all probability produce the same desired effect and further obviate the dangers of residual hydrochloric acid being aspirated from the nasopharynx.

The anesthetic problem deserves special consideration. A new and inexperienced intern is frequently assigned to give obstetric anesthesia. Wider use of local anesthesia would eliminate the dangers of incompetently administered general anesthesia. Too often an active patient is rushed into the delivery room and a general anesthetic started with an opaque mask fastened over the face before information is obtained regarding the condition of the heart, lungs, or stomach. Examination of the heart and lungs is recorded on most labor sheets. The time of ingestion of the previous meal should also be recorded. This would draw attention to the possibility of a full stomach.

Once retching occurs, it is dangerous to force the anesthetic if the stomach has not been emptied. The mask should be removed, vomiting encouraged, and followed by thorough cleansing of the mouth and nasopharynx. Opaque masks are undesirable as vomitus may be concealed. It may also escape recognition if the anesthetist's attention is focused on the obstetric proceedings at the other end of the table. The anesthetist should remain with the patient until the laryngeal reflexes have returned.

Suction, laryngoscopic, and bronchoscopic equipment should be readily available in the delivery room, together with personnel trained in its use. The delivery table should be adjustable for Trendelenburg position.

### Summary

Sixty-six cases of aspiration of stomach contents into the lungs during obstetric anesthesia are analyzed. The incidence of this complication is 0.15 per cent in 44,016 pregnancies at the New York Lying-In Hospital from 1932 to 1945.

Two distinct aspiration syndromes are described. The clinical, roentgenologic, and pathologic features of each are reproduced in the rabbit, and inferences drawn regarding diagnosis, prevention, and treatment.

### Conclusions

1. Gastric retention of solid and liquid material is prolonged during labor.
2. Aspiration of vomitus into the lungs may occur while the laryngeal reflexes are abolished during general anesthesia.
3. Bronchial configuration favors right-sided aspiration. Massive aspiration, however, readily involves both lungs.



## THE MUSCLE OF MICTURITION

### Its Role in the Sphincter Mechanism With Reference to Incontinence in the Female

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AFTER studying the urethra for a number of years, I concluded that, if progress was to be made in the treatment of its disorders, it is essential that a further study of its anatomy and physiology must be made. Therefore the gynecologist must acquire further facts and become more fully equipped if he is to render adequate assistance in cases of female incontinence. Here, I feel that a need really exists for a specialists' study of the anatomy of the mechanism so that one can clearly determine the facts.

To justify this paper, the author presents his method of further studying the anatomy of the urethra and some information which has come to light in this work, which will give us a more intelligent conception of the structure of this important organ. We must consider the physiology, and devote more time to find ways and means of restoring any partial loss of its function. It is desirable, therefore, to take an inventory of facts about the urethra, and then list the items which might be considered incomplete, obscure, or even not known.

1. Are the scattered striated intrinsic muscle fibers in the wall of the urethra separated or divided contracting units, or do they belong to one or more muscles?

2. Are these fibers the extensions of either the levator ani, the bulbo-cavernosus, the ischiocavernosus, or the transversus perinei muscles?

3. How are these muscle bundles innervated?

4. Where is the insertion of that portion of the levator ani which goes to the urethra?

5. Does the urethra possess peristalsis-like organs with similar muscular arrangement, as the intestine and the ureter?

6. Does the urethra pass the urine through it, other than by peristalsis?

7. What is the true sphincter?

8. How is it opened or closed?

9. What is the most probable mechanism of the sphincter?

It is quite clear that, if we are to answer these questions, we must know more anatomy at least, and, probably with it, more physiology.

Suppose we start with the intrinsic voluntary muscle fibers of the urethra and see what previous facts are available. Anatomists and histologists have for years observed striated voluntary muscles to be intimately connected in the urethral musculature. One author describes components of the urethra minutely, and intimates that the urethra consists of two coats of smooth muscle—an outer circular and an inner longitudinal—and that these coats are supported at certain intervals by a collection of striated and smooth muscles. He further

As the uterus was being closed I noted that the patient's respiratory tidal volume was shallow, that the rate was up, and that it was difficult to oxygenate the blood with concentrated oxygen. There seemed to be some form of respiratory obstruction. Filling the bag with pure oxygen produced no effect on the patient's color. The obstruction was not the kind that produces cyanosis or labored breathing, but there seemed to be something interfering with the interchange of air. The patient was laryngoscoped, and I noted gastric contents in the pharynx and dark brown gastric contents escaping from the glottis. I intubated at once a No. 7 endotracheal tube and practiced endotracheal suction, the intubation taking place without any resistance. The glottis was open. Endotracheal suction resulted in the removal of a large quantity of gastric contents from the trachea and bronchi. Respiration improved and the color returned. The respiratory rate remained increased until the patient was returned to bed. Twenty-four hours after operation the patient developed a cough with expectoration, increased respirations, and pain in the chest. Examination of the sputum showed Type XVIII pneumococcus. She was put in a tent and given sulfonamides. In order to raise the tent oxygen concentration two tanks of oxygen were used simultaneously, so that we were using 25 to 30 liters of oxygen a minute. With this delivery a tent concentration of 50 to 60 per cent of oxygen was maintained. In other words, there is no point in giving oxygen unless you are getting a flow which is sufficiently high to reduce the asphyxiation. The respirations throughout were never labored, nor did they exceed 32 a minute. There was no bloody expectoration, and the color was satisfactory at all times. The use of the tent was discontinued on January 15, and the patient had recovered completely.

After the patient had been returned to bed there was pronounced aphonia, and she complained of distress on coughing. On entrance to the hospital the hemoglobin had been 60 per cent; it dropped to 47 per cent, and then returned to 60 per cent. An admission the red blood cells had been 3,800,000; they dropped to 2,900,000, and then returned to 3,800,000.

This case suggests the following comments:

The patient was properly prepared for operation, and yet there was enough fluid in the stomach to drown her. Mouth suction should always be at hand during obstetric anesthesia and, by being at hand, it should be turned on, and the suction tube should hang on the operating table where it can be reached and used instantly. It is not a question of merely having the apparatus; it should be on hand so it can be used if necessary.

Aspiration of stomach contents may take place without cough or struggle.

If a mask is strapped to the patient's face, preventing the escape or knowledge of gastric regurgitation, drowning may easily take place.

A laryngoscope should be at hand in every operating room and the anesthetist should be familiar with its use.

An oxygen tent is useless unless it contains the required oxygen. This should be constantly and accurately determined by the attending pneumatologist or pneumatologic technician.

DR. JAMES R. MILLER.—For the last eight years we have had in the Hartford Hospital a well-conducted "pneumatologic" service. During this time we have had 26,764 deliveries with 24 deaths, or 1 per 1115. We have had no asphyxial deaths, although several times a year we come near to it. The anesthetists are under the control of men who are skilled in the use of the laryngoscope, and suction, piped in the wall, is at hand.

There have been six deaths which occurred during or at the time of delivery or soon thereafter. One was in a cesarean section, a cerebral vascular accident; one was in a case of toxemia which should not have been operated upon, but would have died in either case; one was a spinal anesthesia death, in which the procedure was used under the protest of the anesthetist; one was a rupture of the uterus before admission; another was a severe toxemia; and one other was a rupture of the uterus, with possibly an associated aspiration, though no autopsy was done; and the last one died undelivered with a massive pulmonary embolism, proved at autopsy.

We feel very strongly the necessity of having a well-coordinated physician-controlled anesthesia department which is in control of all the pneumatologic and transfusion services.

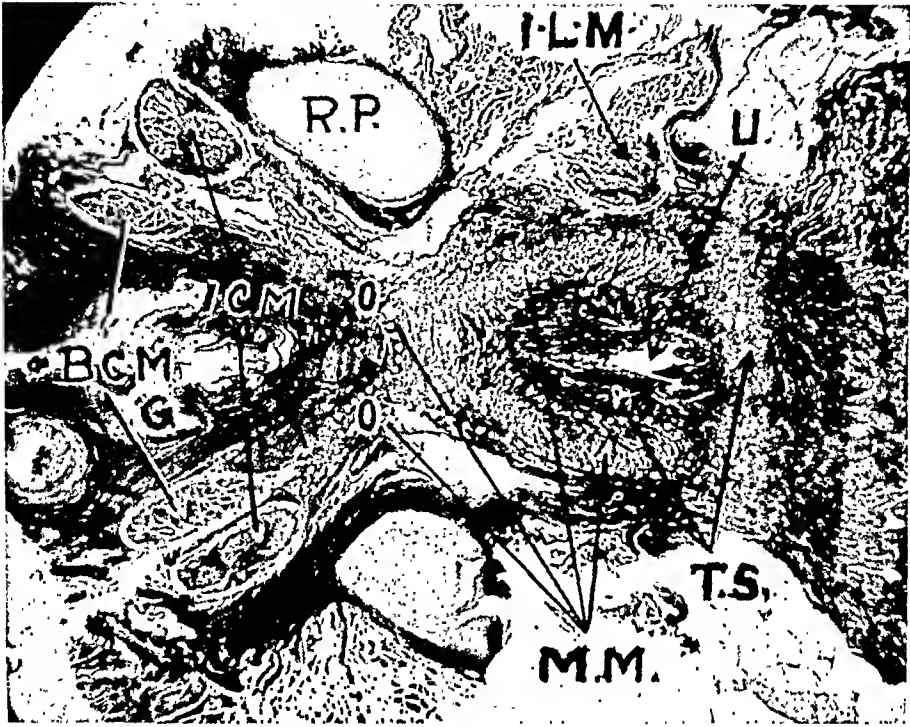


Fig. 1.—Section at right angles to the sagittal plane parallel to the urethral canal through the superior urethral wall.

M.M. = Muscle of micturition (striated). O.O. = Origin of the micturition (striated). B.C.M. = Bulboeavernosus muscle. I.C.M. = Ischioeavernosus muscle. G. = Glandular portion of urethra. I.L.M. = Insertion levator muscle. U. = Urethral canal. T.S. = True sphincter (involuntary, smooth)—circular and longitudinal muscle fibers surrounding the middle and inner two-thirds of the length of the urethra. P.N. = Pudendal nerve trunk. R.P. = Ramus of pubis.

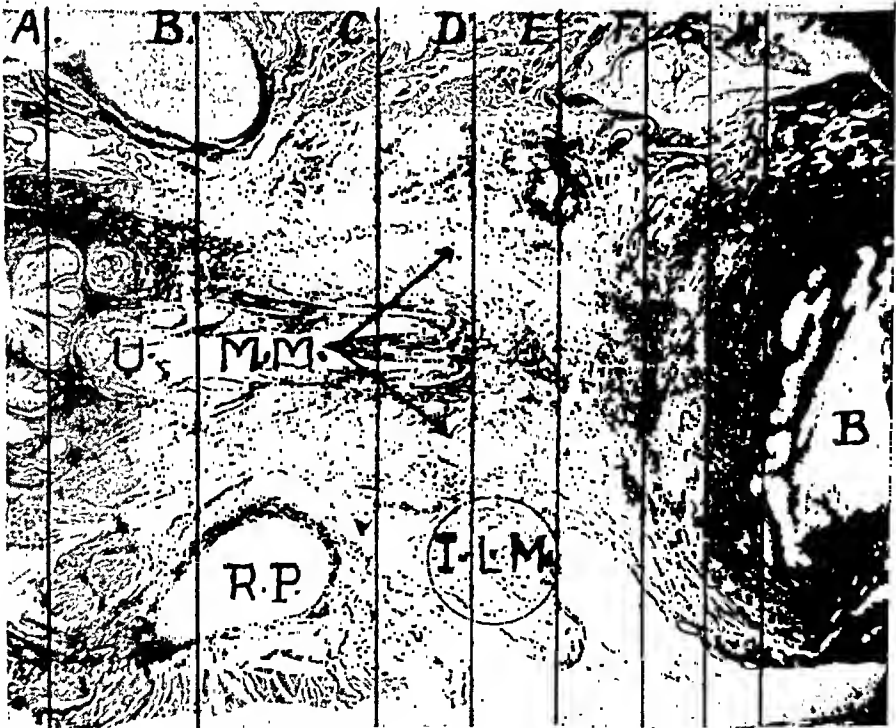


Fig. 2.—Section at right angles to the sagittal plane and parallel to the urethral canal through part of the urethral canal.

M.M. = Muscle of micturition (striated). B. = Bladder. U. = Urethral canal. I.L.M. = Insertion levator muscle. A.B.C.D.E.F.G.H. are lines through which corresponding following histologic sections have been taken. Sections are at right angles to the urethral canal.

says that "certain striated muscle fibers belonging to the group of constrictors of the vestibule also surround and close upon the urethra." Anatomists speak of a voluntary or striated sphincter about the internal meatus, but they have not described any definite muscle. Others mention voluntary or striated fibers running over the urethra, but no fibers below it. One prominent gynecologist in the illustration of his book shows many voluntary fibers surrounding the urethra and many more passing over it to surround the vagina, yet had no definite beginning or ending. Little or no uniformity regarding these muscle fibers can be found, and their action is almost as obscure. Other anatomists believe them to be part of, and continuation of, the levator ani muscles, and if so, then they would constitute an insertion of this muscle. Some commentators would lead one to believe they might come either from the transversus perinei, the bulbocavernosus, or the ischiocavernosus muscles. No definite innervation to the intrinsic muscles has been observed. Until the anatomy is more clarified, the inventory questions remain unanswered.

I could see only one way to clarify this problem, namely, to make an anatomic, histologic study of the urethra in three dimensions. This was accomplished by serial sections of two urethras cut in planes at right angles, one at right angles to the canal, and the other at right angles to the sagittal section of the body, parallel to the canal. First, an adult urethra was obtained and serially sectioned at right angles to the canal. The sections were stained by the von Gieson method. Studying these sections revealed that many striated voluntary fibers passed transversely over the urethra (in the plane between the rami), then down into the lateral walls of the urethra to run posteriorly and obliquely between the longitudinal and circular smooth muscles, and then transversely under the urethra between the smooth muscles of the inner third of the urethra. Two small bundles of muscles jutted off these inferior transverse muscles, posteriorly and parallel to the canal to pass into the longitudinal smooth muscles of the trigone and end there. A full-term baby's urethra was treated similarly and gave similar information. The study was then carried on with one full-term baby's urethra cut at right angles to the canal, and a second parallel to the canal and at right angles to the sagittal section of the body.

Sections parallel to the canal and at right angles to the sagittal section of the urethra illustrate:

1. Two origins of the striated muscle. (Fig. 1.)
2. The nerve supply of the striated muscle. (Fig. 1.)
3. The striated muscle having its own identity separate from the levator ani, the bulbocavernosus, the ischiocavernosus, and the transversus perinei muscles. (Figs. 1 to 9.)
4. A most definite insertion of the levator ani ends in the lateral wall of the urethra not far from the junction of its middle and inner third. (Fig. 6.)
5. The extent of the glandular portion of the urethra (the outer third of the canal) and the relation of the bulbocavernosus muscle to this portion. (Fig. 1.)
6. The extent of the muscular portion of the urethra (the inner two-thirds), and the relation of the striated muscle to this portion. (Figs. 1, 2, 3, 7, 8, 9, 10.)

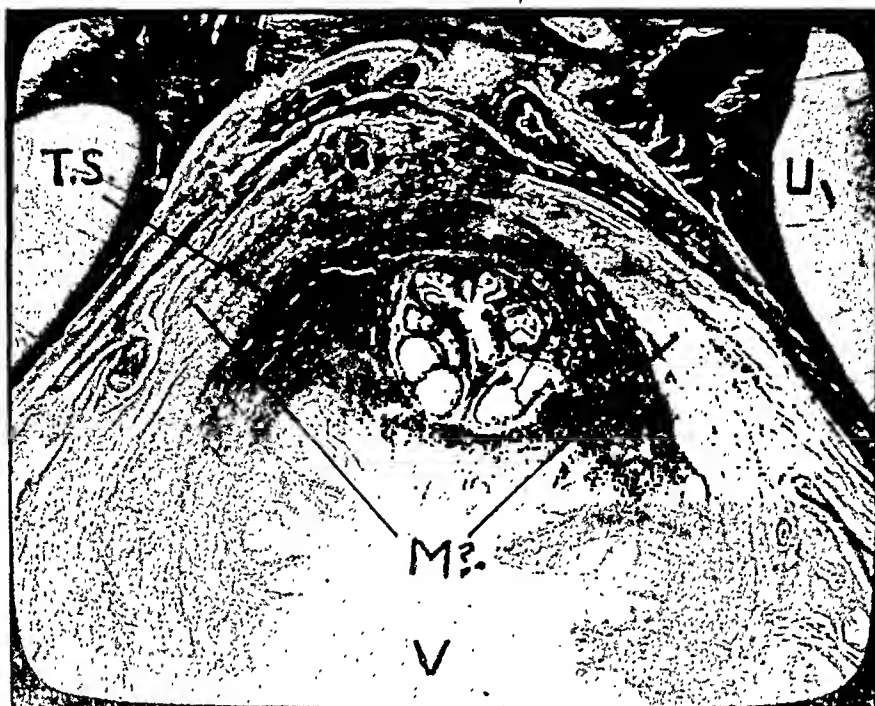


Fig. 5.—Section at right angles to the urethral canal at *B* in Fig. 2.

M.? = This muscle not yet identified but may be part of the bulbocavernosus. V. = Vagina. U. = Urethra (note that much of the glandular portion has been passed and we are entering the true canal). T.S. = True sphincter.



Fig. 6.—Section at right angles to the urethral canal, at *C* in Fig. 2.

M.M. = Muscle of micturition (striated). T.S. = True sphincter. U. = Urethral canal—only a few glands here. SY. = Symphysis. L.M. = Levator muscles. O.O. = Origins of levator muscles. I.I. = Insertions of levator muscles. V. = Vagina. D.D. = "Dimples"—vaginal mucosa.

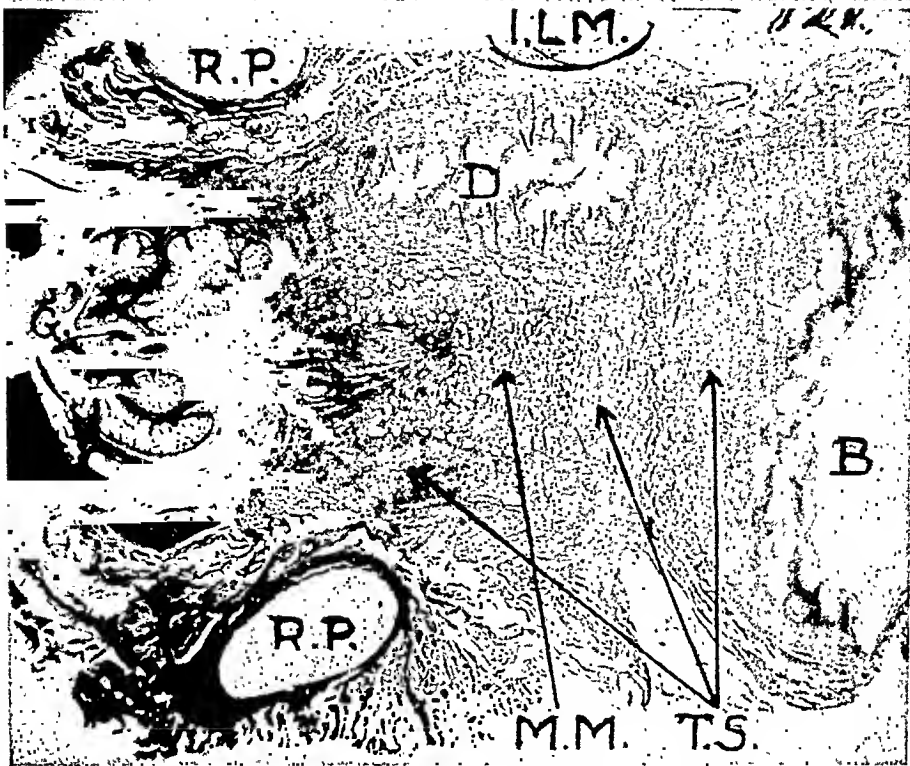


Fig. 3.—Section at right angles to the sagittal plane parallel to the urethral canal and through the inferior urethral wall.

M.M. = Muscle of micturition (striated); fibers run transversely and inferiorly. B. = Bladder. T.S. = True sphincter (involuntary, smooth)—circular and longitudinal muscle fibers surrounding the middle and inner two thirds of the length of the urethra. R.P. = Ramus of pubis. D = "Dimple"—vaginal mucosa. I.L.M. = Insertion of levator muscle. G. = Glandular portion of urethra.



Fig. 4.—Section at right angles to the urethral canal at 4 in Fig. 2.

I.C.M. = Ischiocavernosus muscle. B.C.M. = Bulbocavernosus muscle. U. = Urethra glandular portion. V. = Vagina (fourchette).



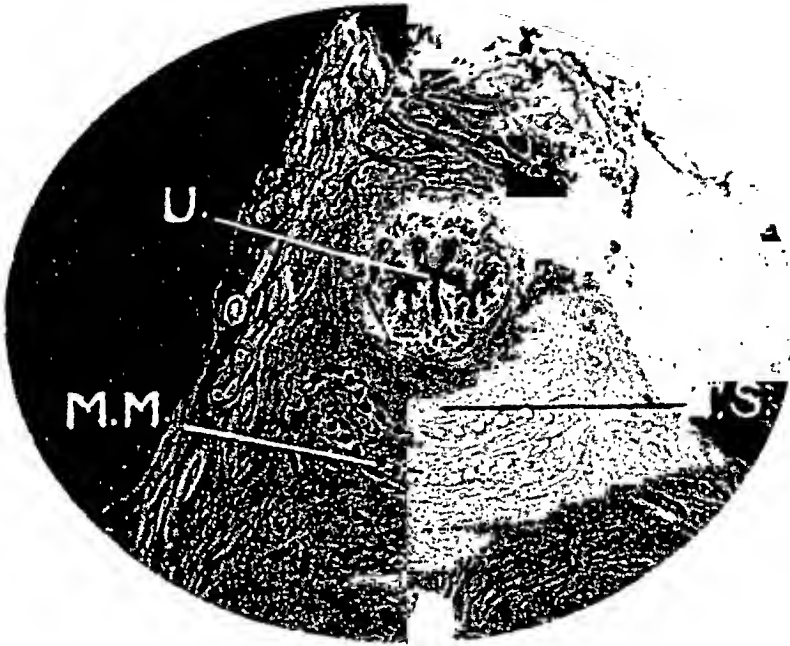


Fig. 9.—Section at right angles to the urethral canal at *F* in Fig. 2.  
M.M. = Muscle of micturition (striated); all fibers in the inferior wall. U. = Urethral canal. T.S. = True sphincter (smooth); many circular fibers.

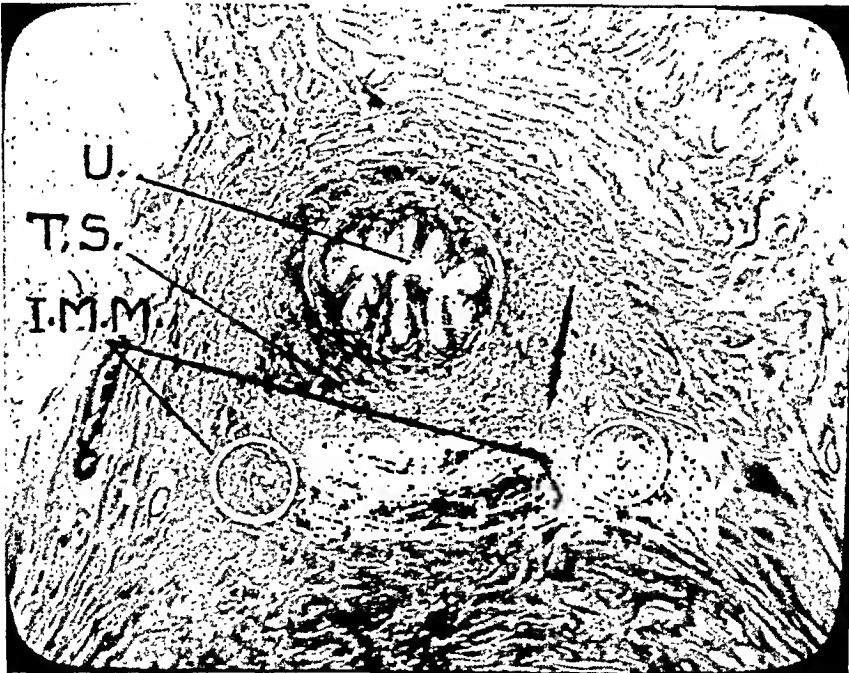


Fig. 10.—Section at right angles to the urethral canal at *G* in Fig. 2.  
I.M.M. = Insertions of the muscle of micturition (striated)—interwoven with the longitudinal smooth muscle fibers in two small bundles. U. = Urethral canal—rather more undulated mucosa. T.S. = True sphincter—has here its greatest number of circular fibers.

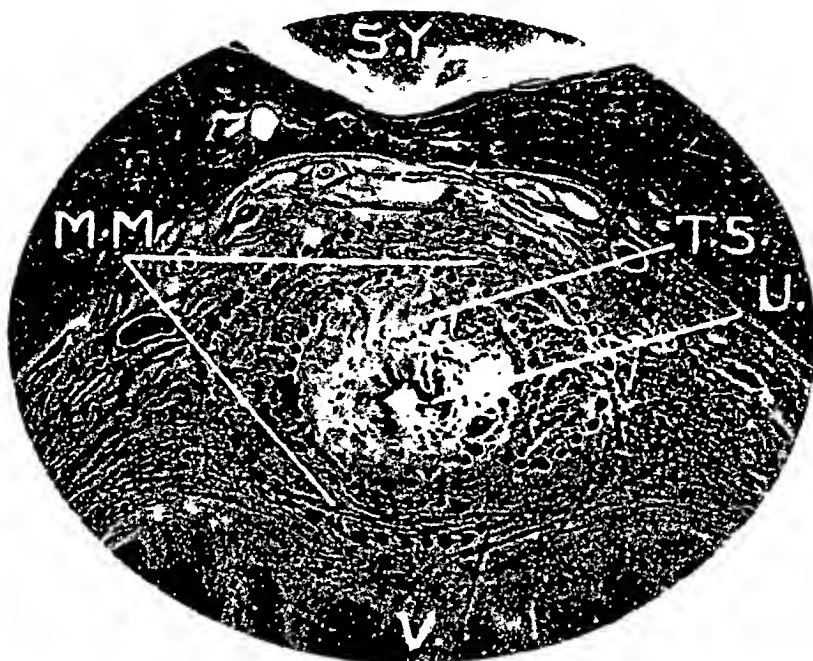


Fig. 7.—Section at right angles to the urethral canal at *D* in Fig. 2.  
 M.M. = Muscle of micturition (striated); more fibers in the superior wall. S.Y. = Symphysis. U. = Urethra. V. = Vagina. T.S. = True sphincter (smooth).

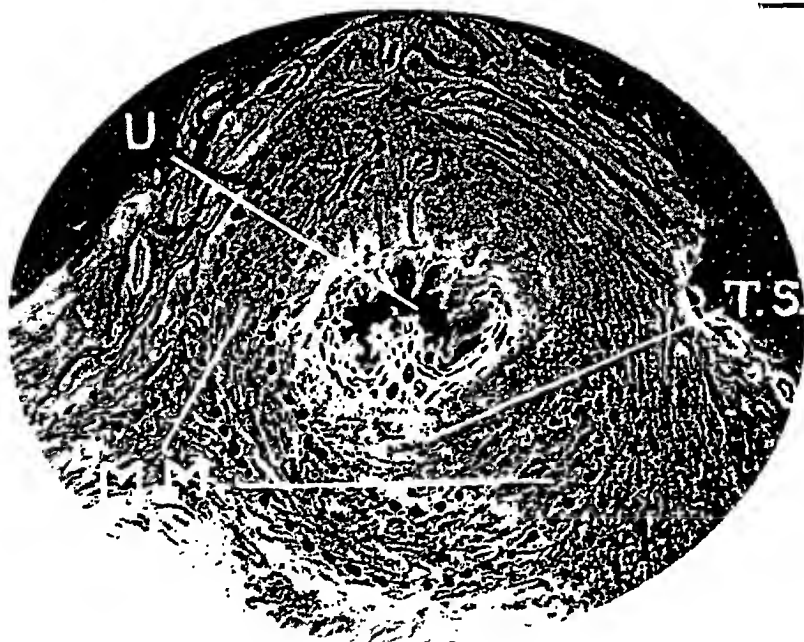


Fig. 8.—Section at right angles to the urethral canal at *E* in Fig. 2.  
 M.M. = Muscle of micturition (striated); more fibers in the inferior wall. U. = Urethral canal. T.S. = True sphincter (smooth).



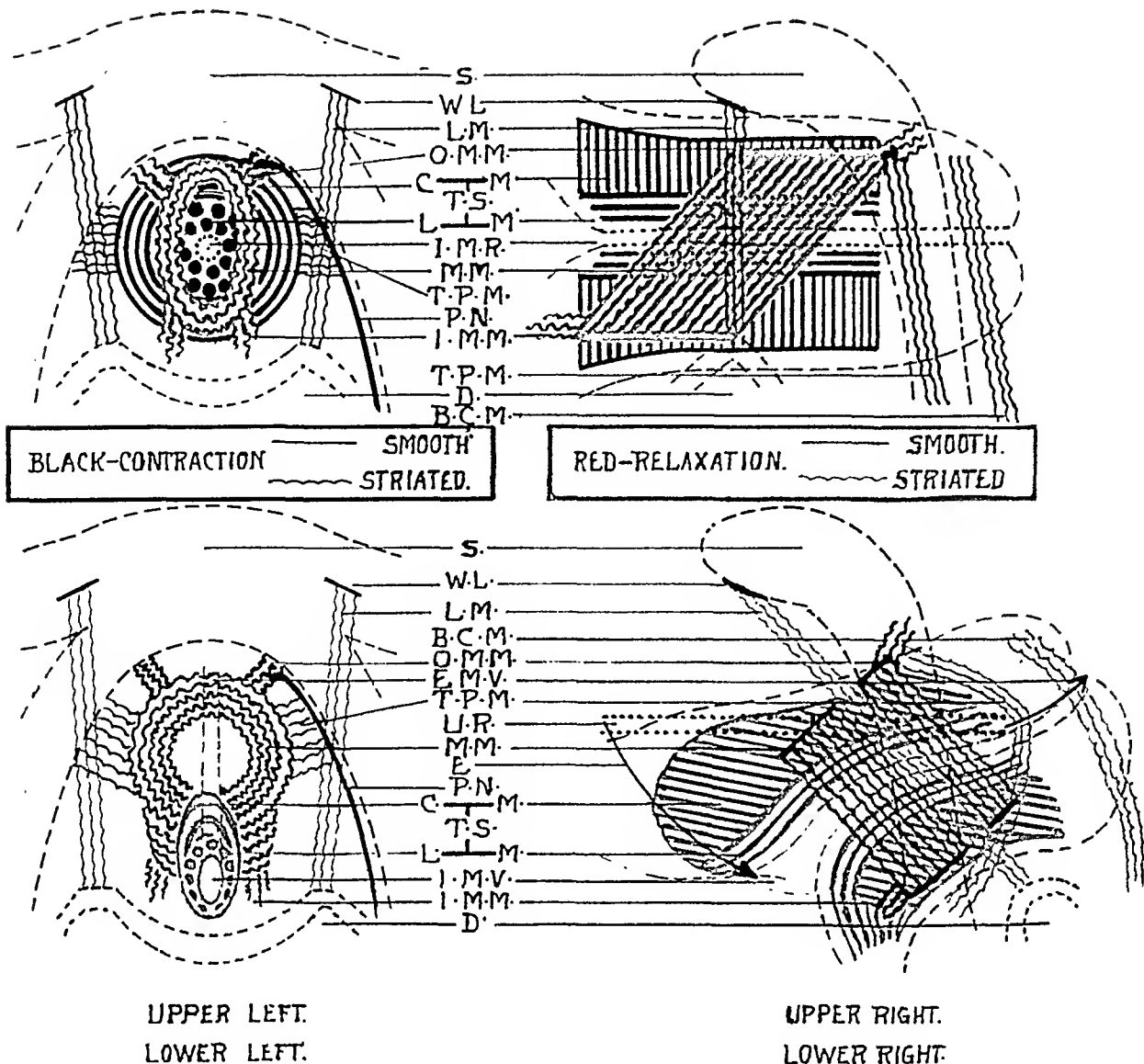


Fig. 12.—Graphic sketch showing muscles of the urethra. Muscles in black in contraction, muscles in red in relaxation, smooth muscles shown by smooth lines, and striated muscles shown by wavy lines.

Upper left—end elevation of the urethra when the muscle of micturition is relaxed. Upper right—lateral elevation of the urethra when the muscle of micturition is relaxed. Lower left—end elevation of the urethra when the muscle of micturition is contracted. Lower right—lateral elevation of the urethra when the muscle of micturition is contracted.

Upper left and upper right. S. = Symphysis. W.L. = White line. L.M. = Levator muscle (striated, contracted). O.M.M. = Origin of the muscle of micturition. T.S.C.M. = Circular muscle of the true sphincter (smooth, contracted). T.S.L.M. = Longitudinal muscle of the true sphincter (smooth, contracted). I.M.R. = Internal meatus of the urethra ("relaxing"). The external meatus appears at the opposite end. M.M. = Muscle of micturition (striated, relaxed). T.P.M. = Transversus perinei muscle (striated, contracted). P.N. = Pudendal nerve branch—innervates the muscle of micturition. I.M.M. = Insertion, muscle of micturition. D. = "Dimple." B.C.M. = Bulbocavernosus muscle (striated, contracted).

Lower left and lower right. S. = Symphysis. W.L. = White line. L.M. = Levator muscle (striated, relaxed). B.C.M. = Bulbocavernosus muscle (striated, relaxed). O.M.M. = Origin, of muscle of micturition. E.M.V. = External meatus urethra ("voiding"). T.P.M. = Transversus perinei muscle (striated, relaxed). U.R. = Position of the urethra when "relaxing." M.M. = Muscle of micturition (striated, contracted). E. = Excursion of the internal meatus of the urethra from its position "relaxing" to its position "voiding." A simultaneous excursion of the external meatus is shown by the arrow at the other end of the urethra. P.N. = Pudendal nerve. T.S.C.M. = Circular muscle of the true sphincter (smooth, relaxed). T.S.L.M. = Longitudinal muscle of the true sphincter (smooth, relaxed). I.M.V. = Internal meatus of the urethra ("voiding"). I.M.M. = Insertion, muscle of micturition. D. = "Dimple."

#### Muscles of the Urethra.

M.M.—Opponents	L.M.	} Striated
	T.P.M.	
	B.C.M.	
	T.S.C.M.	} Smooth.
	T.S.L.M.	

Synonymous terms; "resting, in relaxation, in extension," describing the urethra in this paper are opposite to the synonymous terms; "voiding, in contraction, in flexion."

7. The abundance of the circular smooth muscle in the bladder and urethral walls adjacent to the internal meatus. (Fig. 9.)

8. The abundance of autonomic ganglia which send neurones to the smooth muscle of the bladder and the urethra.

Sections at right angles to the urethral canal demonstrate:

1. Where the striated muscle runs in relation to the smooth muscles. (Figs. 1-10.)
2. Where the striated muscle has its insertions. (Figs. 9, 10.)
3. Where the levator muscle has its insertions. (Fig. 6.)
4. The very meager connection of the urethra to the symphysis. (Figs. 6, 7.)
5. The intimacy of the urethra to the anterior vaginal wall. (Figs. 6-9.)
6. The loose connection between the anterior vaginal wall and the trigone of the bladder. (Fig. 11.)



Fig. 11.—Section through the wall of the internal meatus of the urethra, at right angles to the canal at *H* in Fig. 2. The bladder is beginning here.

I.M.M. = The last bundle of the insertion of the muscle of micturition (striated). U. = The urethral canal opening into the bladder. T.S. = True sphincter (smooth) in the inferior wall of the urethra; it rests on the anterior vaginal wall. C.P. = Cleavage plane between the trigone and the anterior vaginal wall. A.V.W. = Anterior vaginal wall.

The muscle micturition is graphically illustrated in end and lateral elevations by line drawings in Fig. 12. When the true sphincter is circular and possesses sphincter control, the muscle of micturition is relaxed, oblique, and elliptical. When the true sphincter becomes oblique and is deprived of its sphincter control, the muscle of micturition is contracted and circular.

### The True Sphincter

After assaying the muscles surrounding the urethra, the author has come to the conclusion that urine is held in the bladder *wholly* by the circular smooth muscle surrounding the inner two-thirds of the urethra, together with its as-

The muscle, when relaxed, has the shape of an oblique cross section of a cylinder, but when it contracts it takes on the shape of a normal straight cross section of a cylinder. A nerve from each pudendal trunk seems to pass to the muscle of that side near its origin.

When the muscle of micturition relaxes:

1. The levator ani muscle contracts to lift the lateral wall of the urethra near the junction of the middle and inner third of the urethra, or the lateral wall of the cylindrical or true sphincter.
2. The bulbo cavernosus muscle contracts to pull down the glandular portion and compress it.
3. The transversus perinei contracts to give firm support to the urethra at the junction of the outer and middle third of the urethra.
4. The cylindrical or true sphincter is circular in this "relaxing state," and possesses its greatest control.

No urine runs out of the bladder. In this state, the muscle of micturition (the oblique voluntary purse-string muscle) does not exert any distorting influence on the smooth muscle of the cylindrical sphincter.

When the muscle of micturition contracts:

1. The levator ani muscle relaxes and lets the muscle of micturition pull the lower wall of the inner third of the urethra down and out.
2. The transversus perinei muscle is pushed outward releasing any sphincter control, however small.
3. The bulbo cavernosus muscle is pushed outward and up, and releases any sphincter control it may have had.
4. When the muscle of micturition, an oblique, purse-string, striated muscle, contracts it becomes circular to the urethra instead of oblique, and makes a new arrangement of the wall of the urethra. The inferior walls of the inner third of the urethra slide forward almost directly under the superior wall of the middle third of the urethra. None of the circular muscles which, in relaxation, was directly across the axis from its mate is any longer so, but is now diagonally across, the result being a distorted cylindrical sphincter. The cylindrical or true sphincter is now open and permits the urine to run out of the bladder. Any permanent degree of distortion means a similar degree of incontinence. In extreme contraction, all urine runs out of the bladder. At the same time the trigone is drawn toward the transversus inferior muscle of the muscle of micturition. This coincides with the "voiding state" spoken of in the author's previous articles. Again, adhesions may permanently cause some degree of this elliptical formation and therefore some degree of incontinence.

### Conclusions

1. A serial section study of two planes at right angles of any organ of the body having obscure anatomy will yield valuable information.
2. There is need for an advanced anatomic text.
3. The levator ani muscle passes its insertion into the lateral wall of the urethra near the junction of the middle and inner thirds of the urethra.
4. The true sphincter of the urethra is *wholly* composed of the circular smooth muscle surrounding the middle and inner thirds of the urethra, together with their associated longitudinal smooth muscles. When relaxed it may be thought of as a *cylindrical sphincter*. In this "relaxing" state it prevents any urine escaping from the bladder.

sociated longitudinal smooth muscle. I would like to refer to this portion of the urethra as a cylindrical sphincter. Its circular fibers are really circular when relaxed or in the "relaxing" state. The nerve supply is autonomic. The sacral and inferior mesenteric ganglia send neurones to the angle between the ureter and the bladder wall just before the ureter enters the bladder. Here ganglia are established which send neurones to supply the smooth muscle of the bladder and the urethra. Since this arrangement alone (without the muscle of micturition) is somewhat analogous to the intestine and the ureter, urine should be passed through the urethral canal by peristalsis. However, this would take an endless time and would be more or less constant, and Nature has made another provision in the muscle of micturition.

When the muscle of micturition (an oblique, purse-string, striated muscle) contracts, it changes from an oblique to a circular muscle, and, being a purse-string, it distorts the resting urethra, creating a new relation of its superior wall to its inferior wall. The inferior wall of the inner third slides forward to be directly beneath the middle third of the superior wall at the same time that the trigone slides under the superior wall of the inner third, and the circular smooth muscle which constitutes the true sphincter changes from a circular to an elliptical organ with the long axis in the sagittal plane. The sphincter is deprived of its control and permits urine to run out of the bladder. Thus, when the true sphincter is circular, the muscle of micturition is elliptical, continence prevails but, when the muscle of micturition is circular, the true sphincter is elliptical, incontinence prevails. Incontinence will be present in proportion to the amount of elliptical distortion of the true sphincter and will be permanent if the true sphincter is unable to return to its circular stage. Permanent peri-urethral adhesions, the relaxed or distorted true sphincter muscle, the contracted muscle of micturition and the cystocele, all contribute to permanent incontinence.

Studying both series of slides side by side, one gets the following picture of the striated muscle. Two origins can be seen, each loosely attached to the periosteum of the anterior medial face of the ramus of the pubis about the level of the superior part of the perimeter of the urethra in the plane of the rami. The muscles from these origins pass over the urethra transversely, and as they pass laterally they enter the wall of the urethra to pass obliquely and posteriorly as a "purse string" between the circular and longitudinal muscles and, when they reach the inferior wall of the inner third of the urethra, the greater number of fibers pass transversely. Two small bundles jut out posteriorly from these transverse fibers and find their way into and among the longitudinal muscles of the trigone and end there. These two muscle ends are the insertions. For simplicity I will refer to this muscle as the muscle of micturition.

Summing up, the muscle of micturition has two origins, passes completely and obliquely as a purse string in the muscle wall around the middle and inner thirds of the urethra, and has two insertions into and among the smooth longitudinal muscles of the trigone.

## TOTAL ABDOMINAL HYSTERECTOMY\*

### A Study of 500 Cases

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SINCE, in the development of abdominal surgery, hysterectomy first became practicable, there has been a continuous improvement in technique and in mortality. Subtotal hysterectomy was for a long time the standard abdominal procedure and, in many institutions, still is the most frequently performed operation. Vaginal hysterectomy a generation ago enjoyed a considerable popularity, and in the last fifteen years has regained a deserved consideration. In many of the more active clinics of the country, in those cases in which an abdominal operation is preferable, the total excision of the uterus has become more and more frequent. The removal of the cervix has definite advantages, whether it be accomplished by the vaginal or the abdominal pathway. While the proportion of women in whom cancer develops in the cervical stump which remains after a subtotal operation is small, the number of reported cases is large enough to merit attention. Even if we accept the incidence of 2 per cent, which has been given as indicating the probability of the appearance of cancer in the retained stump, the risk is worthy of notice. A second reason exists for the elimination of the cervix. Many cervices are unhealthy. Endocervicitis and eversion often indicate the presence of long-standing infection. Microscopic examination of excised cervices frequently, even in specimens which are definitely benign, shows evidence of epithelial activity which is not normal. Epidermidization and metaplasia are frequent evidences of an inflammatory stimulation of epithelial growth, and the obscuring of the normally clear-cut boundary between the portio epithelium and the cervical stroma indicates changes brought about by infection. These cervices which are not entirely normal are often troublesome after a subtotal operation. Discharge, which does not yield well to treatment, is often met with. The poorly nourished stump has a diminished resistance and does not respond as well to the usual forms of treatment as when the entire uterus is present. Bleeding is sometimes seen. The removal of the stump is sometimes indicated. For both of these reasons the elimination of the cervix seems desirable provided it may be accomplished without increase in the mortality rate, or, in any event, an increase not greater than the number of cases of stump cancer would account for. Fortunately, in well staffed clinics, this is entirely possible. I am not in agreement with an opinion recently expressed, that the total operation should be recommended for all operators. My purpose, in this communication, is to indicate what may be done by a group of trained men. The series here discussed was cared for by a small group of men, all of whom belong to the department of gynecology and obstetrics of Northwestern University.

\*Presented before the 573rd regular meeting of the Chicago Gynecological Society, October 19, 1945.

5. A study of the urethra with serial sections, concentrating specifically on the intrinsic voluntary muscle fibers, reveals that they compose a single muscle, having an unusual shape and as unusual a function. It has been temporarily named the *muscle of micturition*.

6. The muscle of micturition has two origins, possesses its own identity, is entirely independent from and opponent to the levator ani, the bulbocavernosus, the transversus perinei, and the ischio cavernosus muscles, and has two insertions. Two nerves supply it, passing in near its origins, one branch each from the pudendal trunk ascending parallel to the ramus of the pubis. Its function, when contracting, is to distort and open the true or cylindrical sphincter.

7. When the muscle of micturition relaxes, the true or cylindrical sphincter exhibits its maximum control and no urine runs out of the bladder. When it contracts completely the cylindrical sphincter is distorted into an oval formation throughout its length. In this "voiding" state all the urine can escape from the bladder. If complete contraction becomes permanent, complete incontinence exists. Any permanent partial contraction will carry with it a corresponding degree of incontinence.

8. Should the muscle of micturition become devoid of innervation, the cylindrical sphincter would remain closed, and only peristalsis or bladder pressure would carry urine out of the bladder.

9. To obtain maximum restoration of continence it behooves the operator

- a. To restore completely the relaxation of the muscle of micturition by putting the internal meatus of the urethra as far back in the pelvis as possible.
- b. To restore as completely as possible the contracting power—at rest—of the levator ani, the transversus perinei, and the bulbocavernosus muscles.
- c. To restore as much as possible all damage inflicted upon the trigone, the adjacent bladder wall, and the associated anterior vaginal wall, a procedure which is necessary for maximum efficiency of the cylindrical sphincter.

10. To achieve continence of urine it is necessary to maintain this restoration.

The author wishes to thank Dr. Albert H. Aldridge, Chief Surgeon of the Woman's Hospital for the privilege of carrying on this study, Dr. Leon Motyloff and Dr. Grete Stohr for their suggestions from time to time, and others who have in some way contributed to this work.

first twenty-four hours, causes the case to be included in the morbid list. According to this standard, 141 patients, or 28.2 per cent, had a morbid recovery.

A standard as rigid as this, although entirely just, necessarily increases the percentage of morbidity. None the less, a widely used standard is of value as it enables comparisons to be made on a common basis. Many patients, who were in the morbid list, had a rise of temperature over 100.4° F. only two or three times and had very smooth convalescences. Serious morbidity was exceptional.

It should be recognized that, in vaginal and total abdominal hysterectomy, the vagina is opened. Careful preoperative preparation, which should always be done, cannot produce complete asepsis. In subtotal hysterectomy, if amputation is done below the level of the internal os an area which is bacteria laden is traversed. In all total hysterectomies, either from above or below, and in some subtotal operations, a nonsterile field is traversed.

Thrombophlebitis occurred three times, one of these patients being very sick. Recovery took place and the patient left the hospital on the sixty-fourth day. In the other two, convalescence was only moderately prolonged.

In one case total hysterectomy was done because of rupture of the uterus occurring in labor at term. A tear extended from the tip of the cervix to the left lower posterior part of the corpus. The tear was about five inches in length. The patient recovered.

In two cases ureteral injury occurred, in one case the ureter being tied while in the other it was cut. Both patients recovered, although nephrectomy was needed in both cases. The bladder was opened four times. Immediate suture was done and a permanent catheter put in. All of these recovered without trouble.

One of the deaths was caused by septicemia, a tracheobronchitis being also found at autopsy. The other death was from uremia with failure of urinary secretion. Cystoscopy and catheterization of the ureters proved the absence of ureteral obstruction.

In common with the majority of clinics today we believe in conservatism in dealing with the adnexa. In 239 cases the adnexa were not disturbed on either side, while in 136 more the ovary and tube, or at least the ovary, were left on one side. In 375 cases, therefore, both ovaries, or one ovary, remained. The advantage of this is too well understood to require elaboration. On the other hand an unhealthy ovary, or one of which, because of extensive resection, only a small part remains, is better removed entirely.

In 136 cases the appendix was recorded as having been removed; in 189 it was not removed; in 157 cases it had been removed previously; while in 18 cases the history failed to give clear information concerning the appendix. In one of the excised appendices a carcinoid was found. A conservative attitude toward the appendix seems wise. If the hysterectomy has been difficult, and no urgent reason appears for appendectomy, it may well be omitted. In only nine cases was any form of vaginal plastic work done. If any notable degree of lack of support of the uterus is found, we prefer to do vaginal hysterectomy unless a valid contraindication is present.

It comprises a series of 500 cases done between the latter part of 1939 and August, 1945. It is interesting that, in the period considered, no case appears which was done by any member of the general surgical staff of our hospital. Only 6 were found done by approved members of a small courtesy group. These were discarded, although a good result was attained in all, in order to attain an accurate estimate of the work of the staff itself. During the period of time covered by this report, 316 subtotal hysterectomies were done and 353 vaginal hysterectomies. This makes a total of 1,169 hysterectomies of all sorts, in 73.8 per cent of which the uterus was completely removed.

The indication for operation in 319 cases was myoma. In many cases more than one indication existed, or, in addition to the principal indication, other conditions were found. Myoma was found together with ovarian cyst, inflammatory disease, more or less extensive, of the cervix, adenomyosis, postoperative adhesions, carcinoma of the corpus, and inflammatory residues. Adenomyosis as the principal indication was found in 52 cases. Functional bleeding called for treatment in 53 cases. In many of these the pathologic report indicated a uterus considerably over the normal size, with increased connective tissue and thickened blood vessel walls.

In 70 cases the condition of the cervix caused a note to be made in the record by either the pathologist or the operator. In arriving at this number, simple erosion of moderate degree was excluded and those cases in which the cervix was definitely unhealthy were counted. Among the cervical lesions were eight cases of stenosis in one of which a pyometra had been present. This had been relieved by dilatation and drainage some time before operation which was done to prevent inevitable recurrence of the obstruction.

Carcinoma of the corpus was found 27 times. Sarcoma of the uterus occurred once. Endometriosis appears as the primary indication for interference 35 times.

During the period under consideration technique has remained practically constant. With increasing experience the more extended operation was carried out with but little more effort than the subtotal one which had been the routine operation until a few years ago.

The frequent use of the total operation can be justified only if it can be done without increasing the mortality. If an increased mortality rate occurs, especially if it is sufficient to neutralize the incidence of carcinoma in the retained stump, the argument that it protects against cancer falls to the ground. In the series here reported there were two deaths, a mortality rate of 0.4 per cent. In another paper, in a series of 744 subtotal hysterectomies, we showed a mortality of 0.66 per cent. Obviously the danger is not increased under the conditions under which these operations were done. Without a thorough familiarity with pelvic anatomy and technique, there is a very definitely greater danger in the total operation. Among these particularly are injury to the urinary tract and hemorrhage.

Morbidity was estimated according to the rule of the American College of Surgeons, a rise of temperature to 100.4° F. on any two days, excluding the



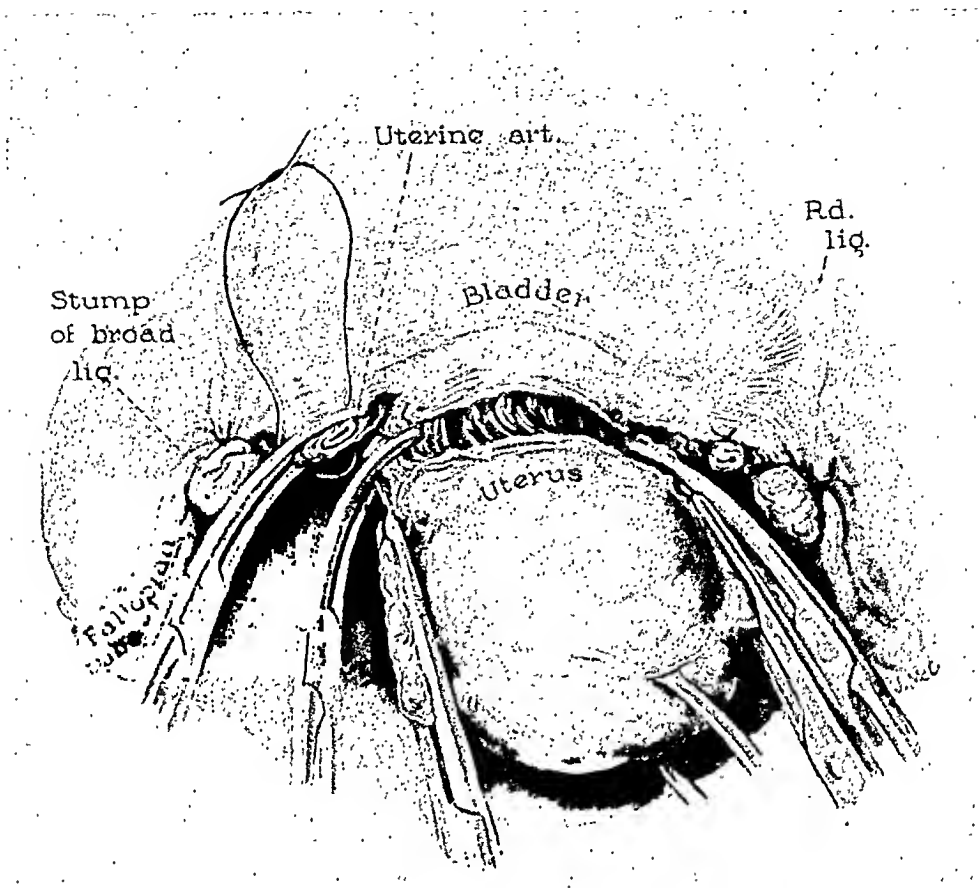


Fig. 2.

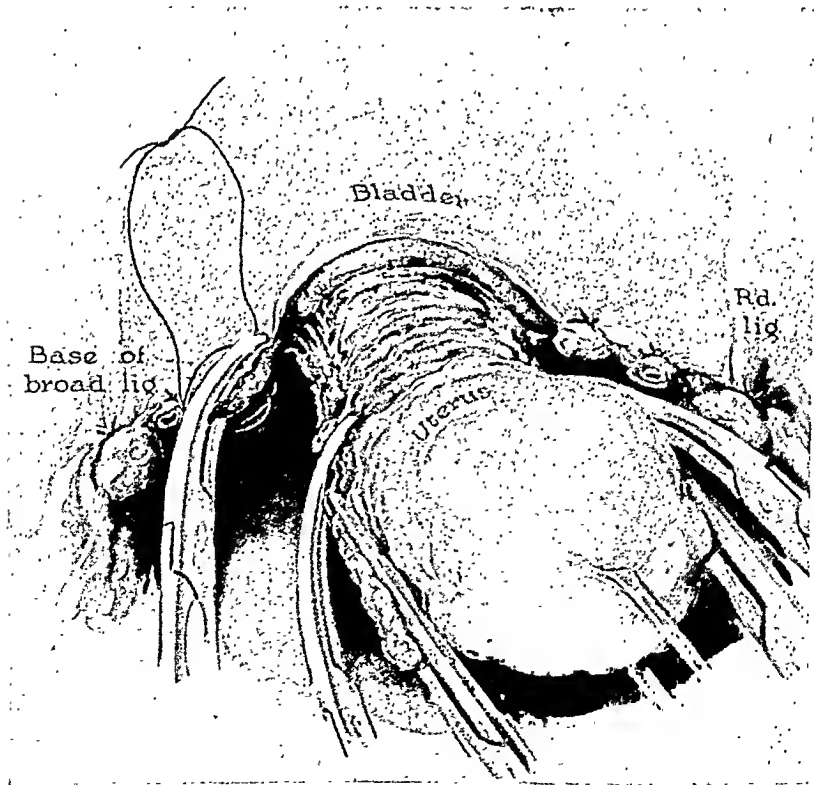


Fig. 3.

Technique, in most cases, is relatively simple. If the adnexa are to be preserved, two straight eight-inch clamps are placed close to the uterus on the broad and round ligaments and including the tube. The broad ligament is divided between these, and the outer clamps replaced by a figure-of-eight suture ligature. This is repeated on the opposite side. The uterovesical fold of peritoneum is opened and the bladder separated downward from the lower part of the uterus and the cervix. The uterine arteries are then isolated and tied.



Fig. 1.

Another clamp is usually needed below the level of the uterine artery. All clamps are at once replaced by suture ligatures. The base of the broad ligament is then grasped by means of a short-jawed, moderately curved clamp which is ordinarily used for vaginal hysterectomy. This is replaced by a suture ligature. The vagina is then opened, cut around, and the uterus removed. If care is taken at this point to enter the vagina close to the cervix, and to divide the vaginal wall flush with the cervix, the vagina need not be shortened.

In most cases the operation is practically bloodless until the vaginal wall is divided. Some bleeding always occurs at this point whether the hysterectomy is being done from above or below. It is not great in most cases and is soon controlled by the suture closing the vagina.

The base of the broad ligament is attached to the vaginal angle by a single suture on each side and the vagina is closed. Experience with both interrupted and running sutures for closure indicates the superiority of the latter.

Peritonealization is carried out by means of the vesical flap of peritoneum. Satisfactory closure is almost always attained. When peritonealization is difficult, as in some cases of extensive inflammatory residues, the sigmoid may be utilized. If attached by a few interrupted sutures of fine gut, and not angulated, its function is not disturbed. In cases in which an irregular mass of myomas must be dealt with, or when extensive adhesions are present, and occasionally in the presence of extensive endometriosis, amputation at the level of the internal os is helpful. The remaining cervical stump is usually then removed easily. This is done occasionally, when it seems likely to simplify the operation.

Number one chromic gut, used singly, is amply strong for sutures and ligatures. For small bleeding points on the vaginal vault, and for ligatures in the abdominal wall, number 0 is used. The use of unnecessarily heavy gut, or of double strands of gut, interferes with healing and is not needed either for apposition or for hemostasis.

The criticism is sometimes made that total hysterectomy shortens the vagina. This, in our experience, is not true. If the vaginal wall is cut through, in removing the cervix, close to the cervical wall, shortening does not occur. A recent and excellent text contains a drawing, illustrating total hysterectomy, in which a cuff of vaginal wall of some size is being removed together with the uterus. If this is done, it is obvious that the vagina is shortened. Division of the vaginal wall should be made close to the cervix.

It is important, whether the total or the subtotal operation is done, that the ovaries be left freely movable and with a good blood supply. Firm attachment of the retained adnexa, either to the cervical stump or to the vaginal vault, is not wise. The broad and round ligaments are put upon tension which may cause dyspareunia, and the blood supply of the ovaries may be interfered with which will increase the likelihood of later cystic change.

Our experience indicates that, in trained hands, total abdominal hysterectomy may be used frequently or even almost routinely. For safe use an accurate knowledge of pelvic anatomy is needed together with a well-developed technique. In the absence of these the operation carries with it a risk greater than that of the subtotal operation. With the mortality reported here we feel justified in making use of the operation as freely as we do.

Examination of patients later indicates that a vagina of normal depth may be retained. If this is accomplished, and if the broad and round ligaments are not left tightly stretched, dyspareunia does not occur.

The advantages of the complete removal of the uterus, whether done abdominally or vaginally, are sufficient to warrant its frequent use in active services staffed by trained men.

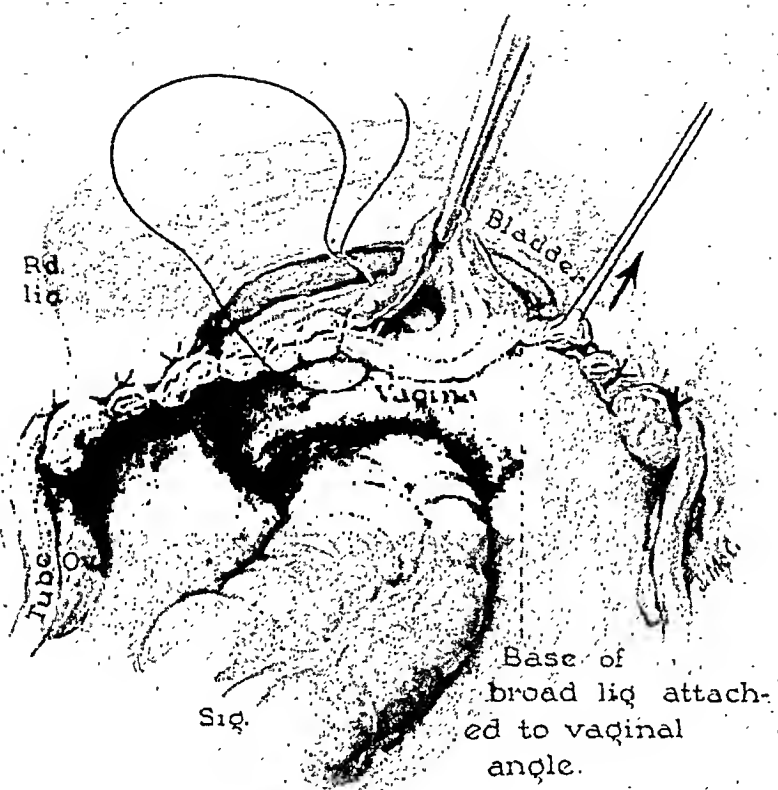


Fig. 4.

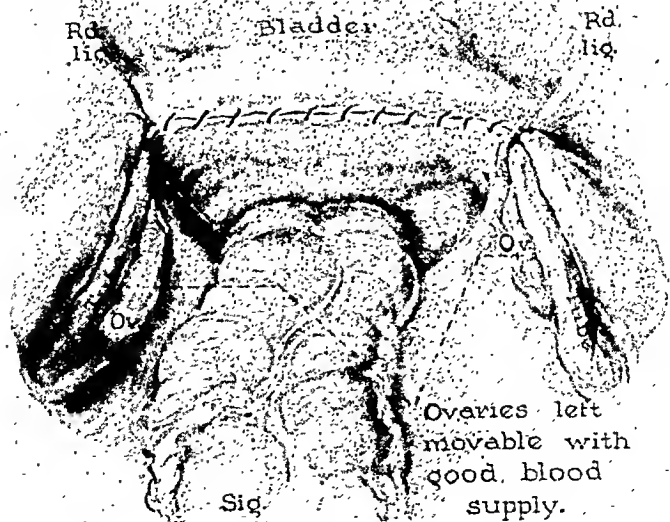


Fig. 5.

DR. IRVING STEIN.—Dr. Danforth's concise report proves that in trained hands, total hysterectomy can be done with a minimal mortality (0.4 per cent). The advantages of removing the cervix and conserving the adnexa when possible are stressed, as well as the necessity of anchoring the vaginal vault with the broad ligaments, rather than the adnexa and round ligaments, which may produce tension.

The question of total versus subtotal hysterectomy has been discussed previously at our meetings, and Dr. Danforth has again shown that good technique, a well-trained staff, and properly selected anesthesia have all contributed to a reduction in mortality and limitation of serious morbidity. I fully agree that the total operation is not to be recommended as a routine for all surgeons, but requires the skill of a specially trained gynecologist. Dr. Danforth beautifully illustrated a workable and adequate technique which enabled him and his staff to accomplish excellent results.

I have employed the Richardson technique by preference in simple cases, but have resorted to variations when large tumors or inflammatory exudates complicated the operation. In some cases, especially where there were fibroids in the broad ligaments, the "key fibroid" principle of Emil Ries is employed. However, my technique differs only in minor details from that described by Dr. Danforth: I use plain catgut instead of chromicized, and as fine a suture as proves adequate. I also employ interrupted circle sutures in closing the vaginal vault rather than the continuous suture, and place a small wick of sulfa-permeated gauze to drain the subvesicle space into the vagina. The drain is removed on the fourth day. I also have used sulfanilamide powder in the peritoneal cavity in some instances; I have noted no harm from its use but am not entirely convinced of the necessity of using this agent to insure smooth recovery.

I recently reviewed 100 total hysterectomies, including 13 Wertheim panhysterectomies; eight of these were done for very early carcinoma of the cervix, four for adenocarcinoma with or without fibroids, one for adenoma malignum of the cervix. In the remaining totals, 80 per cent of the operations were done for fibroids, one for sarcoma of the uterus, four for adenomyosis, and the remainder for miscellaneous diagnoses. The mortality of the entire series was 1 per cent, one patient having succumbed after ureteral injury during the total removal of huge intraligamentary fibroids. There were no deaths after the Wertheim operations.

I fully concur with the opinion expressed concerning treatment of the appendix during hysterectomy and remove it only when it is found to be diseased. In two cases, I have found endometrioma of the appendix. It is very likely that this policy of conservatism in regard to the appendix has resulted in fewer postoperative complications.

In my opinion, the accepted standard of a temperature of 100.4° F. on two successive postoperative days is often of little significance in comparison to the length of the patient's stay in the hospital, as a criterion of morbidity. For practical purposes, morbidity can best be judged on the latter basis. In the 100 cases of hysterectomy which I have analyzed, 52 per cent of those who had total hysterectomy were discharged from the tenth to the twelfth day, 33 per cent from the thirteenth to the eighteenth day, and 15 per cent remained from nineteen to twenty-nine days. In that group where radical Wertheim hysterectomy was performed, three were discharged on the twelfth day, six from the thirteenth to the fifteenth day, and three from the sixteenth to the nineteenth day; only one patient remained thirty-four days. Thus it appears that 15 per cent of the patients were morbid to the extent that their hospital stay was prolonged beyond eighteen days. 85 per cent of the entire group, including Wertheims, had negligible complications, if any.

In the past ten years, I have gradually increased the proportion of totals over subtotal hysterectomies, and, in selected cases, perform Wertheim hysterectomy for early carcinoma. My results warrant a continuation of this policy.

DR. DANFORTH (Closing).—I am rather glad to learn from Dr. Jones that our standard of morbidity is outmoded. I should apologize for forgetting about his presentation. The test is a severe one and gives a rather higher standard of morbidity than we ought to have.

## Discussion

DR. HAROLD O. JONES.—Reports of studies made by groups always yield a pattern of results well worth serious consideration. Dr. Danforth's paper fits into this category. The discussant, however, should not report his results as a comparison, but point out differences of opinion, results, and technique.

The standard of morbidity referred to in this paper is disowned by the College of Surgeons. In our study of morbidity presented to this Society last year, we were unable to find anywhere such a standard. The one referred to was established years ago to apply to uncomplicated delivery of a nulliparous woman. Consequently, it has no relation to any surgical procedure. This is the reason we presented a curve as a norm for morbidity in complete abdominal hysterectomy.

We agree that there should be an ever increasing number of patients of hospital services treated by complete abdominal hysterectomy. In the same way, the number of patients treated by vaginal hysterectomy should increase. These facts, we believe, reflect the progress of the younger men of any group:

Our experience with the occurrence of carcinoma of the cervix has been the same as the author's, and for the same reason sanction the removal of the entire uterus. A more common condition, however, more urgently indicated the removal of the cervix, i.e., chronic cervicitis, where disability is very often exaggerated after operation. The reason offered for leaving an often diseased cervix is that associated conditions have been time consuming, and therefore the operation should be terminated. This we do not believe is often necessary, especially when one considers the fact that almost invariably the associated pathology—residues, or endometriosis, have an almost 100 per cent of diseased cervix. Therefore, in the very condition in which the cervix should be removed, it is often allowed to remain, with its subsequent disability.

Masses densely adherent in cul-de-sac and to the cervix may at times be best treated by opening the vagina anteriorly and removing the adherent tissue from below.

Recently we have seen a patient with an acute ulceration and hemorrhage of the cervix three months after subtotal hysterectomy which could not be differentiated from carcinoma except by biopsy. This tissue also had to be removed.

We would like to ask Dr. Danforth what his impression is as to the number of these patients that had to have cauterization of the vault for granulations? Does he think the type of closure influences this? How many patients had hemorrhages during the hospital stay? Does he get the patients out of bed on the third or fourth day? If so, has it influenced the number of complications? Has he had any eviscerations?

Has the author encountered any prolapse of the vaginal vault in these patients? We have thought the fixation of the uterosacral ligaments to the sutured mucosa a factor of prevention of descent. We agree that complete hysterectomy does not shorten the vagina. If such a condition is found, it quite certainly was present before operation.

We believe Dr. Danforth and others have emphasized the location of the ovaries after operation and made statements which cannot be proved. He stresses that the ovaries lie to the side and free, and cautions about putting them on tension, etc. This fact we cannot support. It seems to us that cystic changes in the ovaries are due to a disturbance in the fundamental circulation to the ovary or its broad ligament anastomosis. I must confess I have put the cervix high in the pelvic plane with tension, and have seen no special pain; I have attached the ovaries well toward the center of the vaginal vault without any disastrous results. As a matter of fact, I would rather believe they do better well suspended than prolapsed into the cul-de-sac.

We have all encountered fistulas of the bladder and ureters. These we believe come from difficult dissection interfering with a terminal vessel in a bladder or ureteral segment with subsequent slough, rather than direct injury.

We conclude with emphasis on Dr. Danforth's opening paragraph to increase the percentage of complete hysterectomies.

# THE MANCHESTER OPERATION, WITH SPECIAL REFERENCE TO PARTURITION AND COMPLETE PROLAPSE

## A Report of 206 Cases

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(From the Department of Gynecology and Obstetrics, St. Catherine's Hospital)

CONSISTENT with general agreement as to the nature of the anatomic supports of the uterus, there has come about, particularly in the last decade, a growing appreciation of the necessity of shortening the elongated transverse cervical or cardinal ligaments in the successful correction of prolapse of the uterus. Based on this principle, the Manchester operation has grown steadily in popularity, yet has not been as widely accepted in the United States as in Great Britain.

Genital prolapse is a comprehensive clinical term for descent of the uterus, as well as all manner of loosening and bulging of the vaginal walls, and lengthening of the portio or supravaginal cervix without prolapse of the uterine body itself. It is obvious that no one operative procedure will correct all these constituents of prolapse. The Manchester operation will not correct enterocele or rectocele; and the only possibility of cure of cystocele is an operation which results in restoration of the bladder floor. Even Donald, Fothergill, and Shaw have not made this plain. Prolapse of the uterus, provided no intrinsic pathology demands its removal, may be corrected by an operation which shortens the cardinal ligaments. And if we are of the opinion that levator and perineal supports are relatively unimportant factors in maintenance of normal uterine position when compared with the upper pelvic floor, then permanent correction of uterine prolapse must be effected by shortening the cardinal ligaments.

My own success with the Manchester operation over a period of twenty-eight years, and the satisfaction of my associates make it difficult for us to reconcile our experience with statements that this operation may not be performed upon women during the reproductive period, or for complete prolapse or proeidentia.

In the United States, just prior to 1932, operations for prolapse of the uterus largely consisted of vaginal hysterectomy, interposition, reconstruction of the vaginal walls combined with intraabdominal suspension, or fixation of the uterine fundus or cervix, or some type of uterosacral or round ligament shortening.

Pemberton<sup>1</sup> performed a combined vaginal and abdominal operation, often with hysterectomy. Miller<sup>2</sup> reconstructed the pelvic diaphragm and suspended the uterus, but recommended in the elderly either interposition or the Mayo vaginal hysterectomy. Counseller<sup>3</sup> reported a large series of 980 cases in which 696 were treated by vaginal hysterectomy. Clute,<sup>4</sup> Laws,<sup>5</sup> Meshburg,<sup>6</sup> Watkins,<sup>7</sup> and Phaneuf<sup>8</sup> favored interposition or vaginal hysterectomy. All these operators performed a combined vaginal and abdominal operation during the child-bearing age. Frank,<sup>9</sup> reporting 480 prolapse operations of which 200 were

Dr. Jones' point that it is important to remove the cervix for infection as well as carcinoma is well taken. Far more often because of infection do we have troublesome cervical stumps later. I have in the hospital now a woman who had had a subtotal hysterectomy done elsewhere and who came in with an infected stump, bleeding profusely.

Granulations in the vagina do occur. I cannot give you any percentage, but I would say that they occur in probably one in four patients. They are not troublesome, as Dr. Stein pointed out. They can be treated by touching with a tiny cautery, such as we use for cervical cauterization without giving the patient any pain, and are very well taken care of in that way.

The number of hemorrhages was not great. We have had fewer since a running suture was substituted for an interrupted one in closing the vaginal vault.

I have not yet tried to get patients out of bed on the third day. They sit up on a back-rest on the third day and go home on the twelfth day.

Dr. Jones' point about the uterosacral ligaments is a good one. The uterosacral ligaments were included in the suture attaching the base of the broad ligament to the vaginal angle.

The ureter has a segmental blood supply and there is sometimes disturbance of this blood supply which may be productive of injury later. Some time ago I had a ureter exposed for four inches. I tied it off and had no trouble.

In broad ligament fibroids the technique as shown on the screen could not be followed. One has to modify it. My own procedure is to split across the top of the broad ligament and enucleate the fibroid before attempting to get the uterine artery on that side. In that way we are far less likely to cut the ureter.

As to sulfanilamide, when it became popular I used it routinely. In the clean cases I could not see much difference. We do not at present use sulfanilamide routinely.

As to drainage, we do not drain at all.



of labor are available, nor is the actual end result known, except in one case in which prolapse recurred. The essential clinical data of the other 5 cases are set down briefly, with age stated as of time of operation. Prolapse did not recur in any case.

CASE 1.—Aged 26 years. Cervix not amputated. Five years later, ten hours of labor with a 9-pound baby; low forceps and episiotomy.

CASE 2.—Aged 34 years. Cervix not amputated. Four years later, five hours of labor with an 8-pound baby; episiotomy only.

CASE 3.—Aged 32 years. Cervix amputated. Three years later, fifteen hours of labor with a 10-pound, 3-ounce baby. Manual rotation of right occipito-posterior, low forceps, and episiotomy.

CASE 4.—Aged 34 years. Cervix amputated. One year later, three hours of labor with a 10-pound, 7-ounce baby. Low forceps and episiotomy.

CASE 5.—Aged 32 years. Cervix amputated. Three years later, twelve hours of labor with a 5-pound, 5-ounce baby. Lower segment cesarean section for rigid cervix.

### Discussion

In young women descent of the uterus is often incapacitating. Complete prolapse, though infrequent, does occur. True, it may be tolerably managed by a pessary, but only with considerable and prolonged inconvenience, discomfort of repeated vaginitis, and no hope of permanent correction. Preservation of the menstrual and reproductive functions is desirable.

The uterus is maintained at its normal level by the fibromuscular structures which traverse the parametrium at the level of the cervical isthmus. Of these the transverse ligaments are the strongest, and so the most important. The round ligaments have nothing to do with uterine support. Ward,<sup>16</sup> who believes that the principle of reefing the cardinal ligaments is a *sine qua non* if the uterus is to be preserved, and others have pointed out that Sims, Emmet, Baldwin, Olshausen, Schroeder, Reynolds, Alexandroff, Dudley, Hertzler, and Halban all utilized this same basic principle.

The combined operation is performed not because it is a satisfactory procedure for correction of prolapse, but to escape the implications of hysterectomy or the Manchester operation. Though direct evidence is lacking, it is likely that shortening of the intraperitoneal ligaments of the uterus does not interfere with parturition, even though vaginal plastic operations are combined with the procedure. The immediate risk of abdominal surgery, its sequelae, and end result often are not taken into account. Of itself, a vaginal plastic operation may cause interference with rotation of the presenting part, or result in such narrowing or rigidity of the birth canal as to make serious trauma or even cesarean section a possibility. Whether it is proper to weigh the risk of abdominal delivery with the probability of recurrence of prolapse after the combined operation is a pertinent question.

### Amputation of the Cervix

If amputation of the cervix has been performed, subsequent pregnancy presents a problem but little different than after the Manchester operation.

ventrofixations, was so discouraged with results that he planned to perform the Fothergill operation in the young, vaginal hysterectomy in the old, and the Le Fort operation in poor risks. Accordingly, in 1935 Frank<sup>10</sup> reported some 200 Manchester operations with very satisfactory results.

According to Goff,<sup>11</sup> Bissell's technique was based upon shortening of the transverse cervical ligaments. To facilitate this procedure he removed the uterus, restricting the operation to women past the menopause and young women in whom prolapse was marked or associated with uterine pathology; results were excellent. And Bullard<sup>12</sup> published well-controlled end results in 361 operations performed by 30 operators at the Woman's Hospital; 95 per cent of these women were cured by vaginal surgery alone, with Bissell's operation showing the highest percentage of success, or 95.8 per cent in 74 cases.

This outstanding success with vaginal plastic surgery was paralleled by Maier and Thudium,<sup>13</sup> who reported, in 1932, 138 Manchester operations performed between 1918 and 1930, with 97.3 per cent successful correction. They had not hesitated to perform this operation upon 47 women in the childbearing age, 11 of whom had children afterward.

In 1933, Shaw,<sup>14</sup> whose paper, no doubt, has had much influence upon American practice, reported 549 Manchester operations with 96.3 per cent success; 27 women had borne children subsequently, five with recurrence of prolapse. He stated that this operation had been performed by a large number of British gynecologists for thirty-five years on all patients with prolapse, irrespective of age or parity.

In 1934, Gordon<sup>15</sup> reported 152 Manchester operations performed between 1917 and 1933; in 50 per cent of these cases the cervix had not been amputated. Excellent results were reported in 94 cases in which observation had been close and personal for two to thirteen years; in 36 cases in which prolapse of the uterus was complete the end result was very satisfactory. There were 22 women in the childbearing age, six of whom were subsequently delivered without recurrence of prolapse. One patient who had had amputation of the cervix aborted twice in the third month. Two of these patients have been delivered again without untoward incident.

During the ten-year period from 1934 to 1943, 236 women were operated upon for prolapse of the uterus in the Department of Obstetrics and Gynecology of St. Catherine's Hospital, Brooklyn; there were nine operators. With few exceptions, all operations were performed under local anesthesia. There were no deaths. The types of operation performed are tabulated:

Manchester	206	
Le Fort	2	
Vaginal hysterectomy	21	
Interposition	7	(one operator)
Total	236	

End results have been studied in many of these cases in order to discover (1) whether the Manchester operation has a place in the management of prolapse of the uterus during the reproductive period, and (2) whether it is effective in the correction of complete prolapse or not.

### Prolapse of the Uterus in Young Women

In this series of 206 Manchester operations there were 36 women less than 40 years of age, 16 of whom were less than 35 years old. Parturition is known to have occurred subsequently in 10 cases. In five of these cases, no details

Fothergill,<sup>29</sup> who did not devise the Manchester operation, but modified and publicized it, reported 32 cases of subsequent pregnancy with one recurrence. Shaw<sup>30</sup> was of the opinion that "the operation does not cause trouble in subsequent labors," but that recurrence of prolapse was a possibility. He reported 664 cases with 24 unsatisfactory results; "5 of these had borne children, and the parturition is most probably the cause of the recurrence . . . there were 30 cases of parturition in the entire series, and of these only 5 showed any sign of recurrence." In 1943 Shaw<sup>31</sup> apparently became concerned about recurrence, preferring not to operate upon young women.

Maier and Thudium<sup>13</sup> reported 47 operations upon women in the child-bearing age; 11 of these women had 13 children, and one aborted subsequent to operation; 10 labors were normal, and three were instrumental; of the 12 women who had labor, the cervix had been amputated in 10 cases. They recommended the operation as a standardized procedure, since 98 per cent of their patients were cured.

Pregnancy after operation, without complication in labor or recurrence of genital prolapse, has been reported by Leventhal and Boshes<sup>32</sup> (1 case) and Salmon<sup>33</sup> (2 cases).

Williams,<sup>34</sup> impressed with the large number of abortions and premature labors occurring after amputation of the cervix, has reported 60 pregnancies in 45 women following the vaginal plastic operation for prolapse which, he states, is standardized in England. Though he does not say so, this is presumed to be the Manchester operation. Pregnancy occurred 49 times in 37 cases in which the cervix had been amputated, terminating as follows: therapeutic abortion, 4; abortion, 20; premature labor, 8; term delivery, 13; not yet delivered, 4. In eight cases, in which the cervix had not been amputated, pregnancy occurred 11 times, terminating in abortion, 2; term delivery, 6; and still undelivered, 3.

Herzfeld and Tod<sup>35</sup> reported 11 pregnancies subsequent to 132 Manchester operations, with eight normal and three instrumental deliveries, and one recurrence of prolapse.

Our South American colleagues have great appreciation of the Manchester operation, and have had long experience with it. Bazan and Althabe<sup>36</sup> believe that this operation is superior to other methods of surgical management of prolapse in the reproductive age. In 354 cases, they report eight pregnancies subsequently; seven of these women delivered themselves spontaneously, and in one case forceps delivery was indicated for pulmonary tuberculosis. Borrás<sup>37</sup> performed the Halban operation in 293 cases, and the Manchester operation in 145, with five recurrences in the first group and two in the latter. Results were highly satisfactory. Subsequent pregnancy and delivery occurred in four cases, but whether after Halban or Manchester is not clear.

At this point it should be said that the Halban operation, as described by Mestitz,<sup>38</sup> so popular in Germany and South America, differs but little from the Manchester operation. The incision for approach to the parametrial tissue is practically the same, yet high vesical fixation with amputation of the cervix is performed if retroversion remains otherwise uncorrected. Mestitz found this operation "unusually satisfactory . . . not only for menstruation but also and especially for pregnancy, labor, and the puerperium. A large series of patients have now been carried through pregnancy, labor, and the puerperium without the development of any pathology or dystocia ascribable to this operation." Schmid<sup>39</sup> elected the Halban operation in 605 cases; only four cases of pregnancy were known to have occurred in twelve years, yet he pointed to the reports of Halban and Mestitz that no trouble of any kind has followed pregnancy.

Rawls<sup>17</sup> and Hunter<sup>18</sup> have shown that there is a very definite risk in pregnancy and labor following amputation of the cervix. If abortion, which is frequent, should occur, there is increased liability to retention of placental tissue and sepsis. In labor, partial or complete failure of cervical dilatation may occur, even rupture of the uterus. Whether part of the combined operation or the Manchester, amputation of the cervix is not a good operation for women in the reproductive period.

But the cervix need not be amputated in the Manchester operation, even though prolapse should be complete. The cardinal ligaments may be shortened otherwise. It may perhaps be necessary to perform reduction of the portio, but it is my practice not to amputate the cervix when performing the Manchester operation upon young women. Presence of the cervix, after restoration of the upper pelvic floor, helps to prevent displacement of the uterine body into the vaginal axis, thus decreasing the risk of recurrence of prolapse. Hunter,<sup>18</sup> who collected a number of cases of dystocia following amputation of the cervix, modifies the Manchester operation in young women by resecting a circular cuff of mucosa just above the portio, before removal of the triangular flap, in order to facilitate approach to the cardinal ligaments.

### The Combined Operation

Richardson<sup>19</sup> advises the combined operation, but believes that the question of sterilization is a pertinent one. Phaneuf<sup>20</sup> says that "It is conceded by most gynecologists that, with few exceptions, young women in the childbearing age should be treated conservatively . . . the operative procedures are fairly well standardized and consist of vaginal plastic repair and intra-abdominal suspension of the uterus;" after the menopause he prefers the Manchester operation. It is the opinion of TeLinde and Richardson<sup>21</sup> that when it is desirable to preserve the function of childbearing, women "are best treated by the combined procedure of a suitable vaginal plastic repair combined with some type of intra-abdominal operation." Recently, however, TeLinde<sup>22</sup> has said that he "performs a round ligament suspension for prolapse only when forced to in young women who insist on further pregnancies, realizing that any type of round ligament shortening is not the best for uterine prolapse and that eventual recurrence of the descensus is probable."

There are no reports of end results after the menopause, and reports of subsequent pregnancy and more immediate end results are scant. Pemberton<sup>1</sup> reported three recurrences after parturition, and Counsellor<sup>23</sup> reported good results in but 60 per cent of 150 cases with recurrence of prolapse in 12 cases, 5 of them following pregnancy.

### The Manchester Operation

Ward,<sup>24</sup> Frank,<sup>9</sup> Kimbrough,<sup>25</sup> Masson,<sup>26</sup> Counsellor,<sup>27</sup> and Tyrone and Weed<sup>28</sup> believe that the Manchester operation has special indications in young women, and advocate it in this type of patient, yet largely their opinions have not as yet been supported by publication of case reports of pregnancy subsequent to operation.

### End Results in Complete Prolapse

In this new series of 206 Manchester operations are 89 cases in which all or part of the uterine fundus protruded beyond the introitus. Enterocoele complicated many of these cases. Clinical prolapse due to hypertrophy of the supravaginal cervix is not included.

An important prerequisite for appraisal of any operation for a complex lesion like genital prolapse is, after selection of the best plastic method for each patient, an accurate detailed description in the case record of the precise anatomic condition before operation. Observation must continue for several years, how many I am not sure. Because of diversified technique and the uneven quality of the operative material, comparisons cannot be fairly made of the results of various operative methods and clinics. Success often depends upon the experience of the operator.

For these reasons, though my associates report satisfaction with their end results, with but two failures to correct uterine prolapse in the entire series of 206 cases, I report the end results in 26 personal cases only, in which prolapse was complete with eversion of the vagina and protrusion of all, or in but a few cases nearly all, of the uterine fundus. In one of these cases, previously treated by interposition, the vagina was completely everted and the interposed uterus entirely outside the introitus. These women have been repeatedly examined by me over a period of years, and in no case has prolapse of the uterus failed of correction. End results are very satisfactory, though not all of these women were found entirely free of minor complaints. In the series of 152 Manchester operations which I have previously reported, there were 36 women in whom complete prolapse of the uterus was corrected. Recently, 14 of these women have been re-examined by me and found to have remained cured.

Not every one has accepted the evidence that the Manchester operation is effective in correction of complete prolapse of the uterus.

Heaney<sup>41</sup> believes that "the operation has no place in the treatment of complete procidentia. If a case of procidentia is to be cured by vaginal operation, the uterus has to be removed." Tyrone and Weed<sup>28</sup> say "its advocacy for procidentia is to be condemned." TeLinde and E. H. Richardson, Jr.,<sup>21</sup> say that the Manchester operation "is nothing more than a radical anterior colporrhaphy. . . . It does very well in the cure of cystoceles with first and at times second degree descensus, but it hardly seems a logical procedure when there is a complete procidentia."

The Manchester operation is a rational procedure for complete prolapse. As a matter of fact, the operation is not only more readily performed in this type of case, and so, more expeditiously, but anatomic identification is more precise. The transverse cervical ligaments are more readily found because of compensatory work, hypertrophy consequent to slow descent or genital prolapse of long standing. The satisfactory end results reported by many operators speak for themselves.

Lacey,<sup>40</sup> in a collective survey of four- to six-year end results of 521 Manchester operations performed at St. Mary's Hospitals, Manchester, England, reported that 382 operations had been performed during the reproductive period. He found that "330 successes bore 67 children (instruments 32 per cent); 19 improved bore six children (instruments 80 per cent); 33 failures bore 16 children (instruments 62 per cent)." To just how many women these babies were born is not stated. He stated that both failures and "improved" show a higher ratio of labors, and again a higher ratio of instrumental deliveries than successes. That is what one would anticipate, and it is obvious that one can scarcely expect a colporrhaphy or any other operation to stand the strain of parturition better than the normal and natural pelvic floor." Fothergill,<sup>29</sup> whose one recurrence occurred after three deliveries, said at the same meeting: "I formerly thought that an operation for prolapse should prevent recurrence even if the patient had one or more subsequent confinements. But we must remember that the arrangements which nature has provided for the support of the pelvic viscera do not by any means always stand the test of pregnancy and labor. To expect from the surgeon arrangements superior to those designed by Almighty Providence, in cases in which these have already failed, is surely asking too much. All we can demand is that the new pelvic floor shall be as good as the original one and a little better if possible."

All of the cases of parturition subsequent to the Manchester operation which I have been able to find after careful search are reported in Table I. In the majority of these reports it was not possible to discover whether cervical amputation had been part of the Manchester procedure or not. The Halban operation is included because it differs but little from the Manchester, and in the report of Borrás the Manchester end results are not separately specified (Table I).

TABLE I.—PARTURITION SUBSEQUENT TO THE MANCHESTER OPERATION

	OPERATION		NO. IN CHILD- BEARING AGE	NO. OF DELIVERIES	SUBSEQUENT RECURRENCE	OPERATIVE DELIVERY
	MANCHESTER	HALBAN				
Maier and Thudium <sup>13</sup>	138		47	13	None	Instrument 3
Shaw <sup>14, 30</sup>	664			30	5	None
Gordon <sup>15</sup>	358		58	18	1	Instrument 8 Cesarean section 1
Hunter <sup>18</sup>	19		19	1	None	None
*Fothergill <sup>29</sup>	156			32	1	Instrument 23
Leventhal and Boshes <sup>32</sup>	51			1	None	None
Salmon <sup>33</sup>	254			2	None	None
Herzfeld and Tod <sup>35</sup>	132			11	None	Instrument 3
Williams <sup>34</sup>	45		45	27	None	None
Bazan and Althabe <sup>36</sup>	354			8	None	Instrument 1
Borrás <sup>37</sup>	145	293		4	None	None
Mestitz <sup>38</sup>		Large series		Large series	None	None
Schmid <sup>39</sup>		605		4	None	None
Lacey <sup>40</sup>	521		382	89	33	Instrument 35

\*Included in Lacey's figures.

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### Summary and Conclusions

1. Methods of surgical correction of uterine prolapse in the United States just prior to the last decade are reviewed.

2. End results of 206 Manchester operations have been studied in order to discover the value of this procedure during the reproductive period. Parturition occurred subsequently in 10 cases. In a series of 152 cases previously reported, eight babies were born to six women.

3. The relative merits of the combined operative procedure and the Manchester operation for the surgical correction of uterine prolapse during the reproductive period of life are discussed. The Manchester operation is recommended.

4. Reports of parturition subsequent to the Manchester operation are discussed and tabulated.

5. Whether the Manchester operation is suitable for women in the reproductive period is a question of great importance since its alternative, the combined operation, is not satisfactory. Operations for correction of prolapse of the uterus are, for the most part, performed after the menopause, and comparatively few cases of subsequent pregnancy have been reported. Up to now, no survey of the entire subject has been made. Some gynecologists remain unconvinced that women may be safely carried through parturition without severe dystocia or serious damage to the plastic end result. Yet many who have performed this operation upon young women have reported no serious dystocia or any pathology in the puerperium. The incidence of forceps delivery may be discounted, since instrumental delivery through a wide episiotomy is advisable after any plastic vaginal surgery. The possibility of cesarean section, though remote, must be taken into account, particularly if the cervix has been amputated. Even complete prolapse of the uterus may be corrected without this dangerous procedure.

6. The Manchester operation has given excellent results in 62 cases of complete prolapse in which observation has continued for long periods of time.

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modern surgical technique that it should be considered wholly obsolete and outlawed. (c) Added to this is the frequent incurrence of such damage to the mother's soft parts as may lead to subsequent tragic gynecic disability.

2. *Cesarean-hysterectomy*, generally historically mistakenly called the Porro operation. This is objectionable in that it is used in already seriously ill patients, necessarily poor operative risks. Under such circumstances it is a formidable procedure, and its immediate mortality must be high. We have no experience with the use of this operation for already existing uterine infection. The Chicago Lying-in service shows a mortality from this procedure of 1.4 per cent. In a comparable table with three other clinics, none approaches this very low figure. One of them is fourteen times that rate, the average more than four times as great, and a collective series attributed to Irving shows ten times that rate.

There is no evidence that these reported series are critically broken down to include only cesarean-hysterectomies performed for fetopelvic disproportion. Diekmann does not even indicate such a breakdown for his own exceedingly low figure. Certainly all of our cases, and doubtless some of his, and those quoted from the other clinics, as well as Irving's series, were done for other indications, which of their own nature contributed importantly to the mortality rates shown. Even this uncritical grouping of cases, however, does exemplify a serious hazard incident to this procedure. Baldwin's results in the treatment of certain cases of puerperal infection by hysterectomy, which Diekmann says prove conclusively that extraperitoneal section is not as safe as cesarean-hysterectomy, actually shows a 25 per cent mortality! Briscoe, quoting Lull, states that the Philadelphia statistics markedly show "the very high death rate from the Porro operation which is usually thought of as the procedure of choice in the infected case." He shows that a ratio of the Porro operation to all sections, of 1.8 per cent, resulted in 10 per cent of all section deaths. Twenty-seven Porro operations showed an absolute mortality rate of 11.1 per cent.

3. *Marsupialization and exteriorization of the uterus*. We have not had, and I hope never will have, any experience with these procedures. I quite concur with Diekmann's statement that they have no place in modern obstetrics.

4. *Exclusion operations*. There is no doubt that these operations have saved many lives. I have felt this to be true in a few cases in my own hands through the years, and Cooke's remarkable series of his own special modification of peritoneal exclusion by utilization of the round ligaments attests the value of such procedures. In our own hands, however, and I think in general experience, it must be conceded that these procedures are unreliable. The suture line, depended upon in all of them for the walling off of an artificial "lesser peritoneal cavity," so to speak, from the general cavity, is not entirely impervious to the transmission of infection, and is frequently injured or torn in the manipulation of extraction. This fact is recognized, for instance, in Irving's expedient of reinforcing the peritoneal suture line by the inclusion of fascia in his "artificial wall." When damage to, or destruction of, this artificial wall does occur, it is apt to be extensive and thus defeat the whole object of the technique. In Cooke's experience, he frankly states that peritonitis in the artificial lesser cavity occurs, and his cases are subjected to a long period of drainage and a greatly increased length of hospital stay.

5. *Extraperitoneal cesarean section*. This operation is by no means new. It was proposed and indeed practiced more than a century ago. An active reemergence of interest in the procedure, with the development of many modifications of technique, occurred more than a generation ago. This interest and practice has continued since that time. During a part of this period American interest centered in the possibilities inherent in the development of the exclusion

## AN EVALUATION OF EXTRAPERITONEAL CESAREAN SECTION\*

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THE major cause of mortality from transperitoneal approach to the pregnant uterus is peritonitis. Thus, in our own service of six deaths following and due to, cesarean section, employed because of fetopelvic disproportion, all were due to peritonitis. All exceeded our own strict standard of conditions to be later specified. Where such approach through the general peritoneal cavity is used in late neglected cases, the mortality is so high as to have been described in the past as "frightful." Where, however, it is reserved for early uninfected cases, mortality in accomplished hands approaches nil.

Of course there have been refinements in the techniques of transperitoneal operation, and some authorities have felt that these refinements, particularly with the use recently of powerful antibacterial agents such as sulfonamides and penicillin, would suffice to overcome the peritoneal hazard of cesarean section, even in cases in which its conditions were not ideally fulfilled. Our own conviction is that this is not true. We recognize the superiority of the newer techniques of lower segment operation so strongly as to have practically outlawed the classical operation in our practice. We do not feel that that technique sufficiently protects the general cavity against infection and the spread thereof. Hence the same restrictions as to the proper applicability of transperitoneal cesarean section apply to the most improved techniques in almost the same degree as to the classical type.

There still remains, therefore, the problem of the elimination of peritonitis from obstetric practice. As has been indicated, no expedient involving the broad invasion of the peritoneal cavity is competent to do so. In relation to cases not exhibiting proper conditions for such operations, several expedients are available.

1. *Delivery of all such cases by the vagina.* This may involve considerable immediate danger, craniotomy applied even to the living child, and a degree of maternal soft parts trauma, inviting disaster just as surely as would unsuitable application of transperitoneal section. (a) That such difficult vaginal delivery is relatively safe is not borne out by experience. Thus, of 101 deaths in our clinic due to purely obstetric causes, 12 patients died of hemorrhage or sepsis directly dependent upon difficult vaginal delivery. This expedient is, therefore, by no means a competent answer to the problem. (b) Besides the immediate dangers inherent in it, as reflected in mortality, there is occasionally involved, when this course is inexorably followed, the deliberate sacrifice of a living fetus. Such a procedure, no matter what the estimated prognosis as to the survival of a particular fetus may be, is so abhorrent to the refinement of

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This is perfectly true. But a sufficiently large number of the many hundreds of cases reported *have been* for demonstrably infected cases, as to have very dramatically demonstrated the value of the operation. Certainly the pioneers in the development forty years ago of the basis of modern practice were sufficiently often confronted by "badly" infected cases to spur their adventure in evolving new techniques. Kusehner (quoted by Ricci and Marr) said in relation to 72 cases reported in 1912, "No degree of infection had contraindicated the operation." Steele said of all his cases that there was "no doubt concerning the probability of infection." Waters reports 90 out of 250 cases definitely showing preoperative morbidity or sepsis. Irwin states that all his cases were "infected, or potentially infected."

Ricci and Marr state that extraperitoneal section "should displace all other types of cesarean in infected and mismanaged cases." Dieckmann speaks of its application to "the infected case," and, in a private communication, implies that its only proper value is in "neglected" patients. Our concept of its value is not so restricted. It is, therefore, desirable that we attempt to define what is meant by "infected," "mismanaged," and "neglected" cases.

We would propose that all cases subjected to cesarean section for fetopelvic disproportion be divided into the following:

#### I. *Clean cases.*—

1. Cases not in labor, nor with membranes ruptured, nor subjected to any manipulation, nor showing any intercurrent infection.
2. Cases same as 1, except with only short period of labor, with membranes ruptured not in excess of a minimal time.

#### II. *Potentially infected cases.*—

1. Those in labor more than twenty-four hours.
2. Those with membranes ruptured more than twelve hours.
3. Those with any other manipulation than a very few rectal examinations and/or one ideally guarded vaginal examination.

#### III. *Actually infected cases.*—

All those which, in addition to the factors constituting potential infection exhibit

1. Exaggeration of those factors, as (a) excessively long, exhausting labor, (b) membranes ruptured two or more days, (c) excessive number of carelessly made examinations, or manipulation embraced in attempt at induction of labor, or artificial vaginal delivery, *plus*
2. Actual clinical signs of infection such as intrapartum chills, fever, rapid pulse, dehydration, follow amniotic liquid, excessive leucocytosis, positive cultures for pathogenic organisms in amniotic liquid or blood-stream.

The worst cases of this group probably constitute what are called the "mismanaged" or "neglected" ones.

Notwithstanding the best programs of community and medical education, maternity services will continue to receive occasionally badly neglected, mis-handled, and already dangerously infected patients, many of these already complicated by hemorrhage and shock. If our idea of what constitutes an infected case embraces only this group, differences in the evaluation of procedures may very well be minimal. This group will show a considerable mortality, no matter what the method of delivery is. We would certainly concur with Dr. Dieckmann in preferring to handle the majority of them conservatively,

operations. For the past fifteen years, however, there has been increased interest in, and use of, true extraperitoneal section, with particular attention to two general types, the Latzko and the Selheim procedures, both of which have been modified and refined by several American investigators.

To our minds, this type of procedure much more nearly fills the need for the protection of the parturient against the risk of fatal peritonitis following cesarean section than do any of the other alternatives already listed.

As evidence of the concurrence in the belief in this value, a very cursory review of recent literature reveals its widespread use.

The belief which I have just expressed in the value of this operation and its apparent sharing by many men, is not shared by everyone. Briscoe says that in the discussion of Lull's paper in 1943, it "was generally agreed that there was little need for the extraperitoneal operation." (It is not implied that this is Briscoe's own opinion.) In his recent most excellent review of cesarean section mortality, William J. Dieckmann concedes that the extraperitoneal section is theoretically ideal, but concludes that this operation is not the proper treatment for the infected case. In support of this conclusion he points out that, due to accidents of technique, the peritoneum is frequently perforated and that once this has occurred, the procedure thereby ceases to be extraperitoneal, and no protective efficacy can be imputed to it.

This is, of course, theoretically true. As a matter of experience, however, it is not valid. The potential or even actual soiling of the peritoneal cavity through a small rent in its lower portion, especially if the chance of such soiling is minimized by the recognition and repair of that damage *before* the uterus is opened, is not greatly hazardous. It is a very different thing from the massive spill of infected amniotic liquid which occurs in transperitoneal operations, no matter how elaborate the packing, or other means of limiting such effect may be, or of the continuing leakage of infective material through a broken-down uterine incision so graphically described by Dieckmann himself. This accidental wounding of the peritoneum is admittedly frequent, but the relative safety of the extraperitoneal operation is too extensively established to be questioned.

Ricci quotes P. Baum, who, in 1923, reported 133 extraperitoneal operations in which the peritoneum was torn in half the cases, with a mortality of 1.5 per cent. Waters in 250 cases found injury to the peritoneum in 27 per cent, with a gross mortality of 0.8 per cent. Irvin reports 285 collected cases by 11 surgeons, in which the peritoneum was opened 50 times (17.5 per cent). There was no peritonitis in these 50 cases, and only one case of peritonitis in the whole series. He adds 32 cases of his own, with the peritoneum opened five times (15.6 per cent) with no deaths. Daichman and Pomerance report 100 cases with 33.3 per cent of peritoneal injury without a death. Aldridge, Bourgeois, ourselves, and others have deliberately wounded and repaired the peritoneum before opening the uterus. All such injuries and repair, at worst, are less extensive and less dangerous than the wounding involved in "exclusion" operations. Dieckmann further says that large numbers of these operations are performed on cases which are not actually infected, and that therefore mortality statistics referable to all operations of this type cannot be depended upon as a valid index of its protective efficacy in badly or actually infected cases.

be tested before labor. So, while we may concur with McKelvey that "The doubtful range is now very narrow," we cannot agree that all in this range should be electively sectioned, and "the test of labor and late section have disappeared." On the contrary, we believe that *all* cases in the "doubtful range" should have the benefit of a test of labor, and Greenhill, in an editorial comment on McKelvey's paper, would appear to favor a test of labor for many of the cases which McKelvey would electively section. If this plan is carried out, procrastination on the basis of reasonably justifiable hope will sometimes lead to disappointment. The case will be thrown into that category unsuitable for transperitoneal section, but definitely requiring abdominal delivery.

Just how narrow is the incidence of such cases? In a survey of labor some time since, we found that 6 per cent of our clinic material remained in labor more than thirty-six hours. Of these, more than a third delivered spontaneously in vertex; about 11 per cent were sectioned. The latter cases would therefore be 0.66 per cent of our total cases. They should all, according to our practice standard, be sectioned by the extraperitoneal method. If to this 0.6 per cent were added the cases between twenty-four and thirty-six hours of labor, the incidence of extraperitoneal section would be somewhat higher. But it is altogether not an especially formidable statistical figure, and is not as large as the number of unnecessary sections done by those who never permit their cases a test of labor.

### Summary

1. There is, as there always has been, a need to protect the parturient woman against peritonitis.

2. No method of transperitoneal approach, except within the rather narrow limits of a strict set of conditions as to time and other factors, is adequate to do this.

3. Other available methods of delivery include (a) delivery by vagina, not always safe for mother or child; (b) cesarean-hysterectomy, mutilating, formidable, dangerous; (c) marsupialization and exteriorization of uterus, appealing so little to good surgical standards as not to rate discussion; (d) exclusion operations, relatively unreliable in efficacy; (e) extraperitoneal section, established by our experience as in a high degree safe and efficacious.

4. A definition of clean, potentially infected, and infected groups is offered.

5. Extraperitoneal section is applicable to the most desperate of the infected group.

6. Its greatest value, however, is in its application to the *potentially* infected group.

7. This group, though of small percentage incidence, is not yet capable of entire elimination from even capable experience.

8. Extraperitoneal section is an important resource of the obstetric armamentarium in the proper management of all potentially infected or infected cases.

with primary attention concentrated on improving the general condition of the patient, in contemplation of vaginal delivery where possible.

But even in this group of cases, when it is necessary to do any supra-symphyseal operation, extraperitoneal section would still appeal to us as giving the patient a better chance of survival than transperitoneal cesarean-hysterectomy, both from the risk of peritonitis and from the fact that the latter operation is surgically more formidable than the former.

But Dr. Dieckmann himself, in his summary, would appear to include a much broader group of cases in those which he is unwilling to submit to transperitoneal section. Thus he states, "Total cesarean section mortality can be kept below 1 per cent by the following evaluation of the case: Are there any of the following contraindications present? (a) Ruptured membranes over twenty-four hours. (b) Labor over twenty-four hours. (c) Repeated rectal or vaginal examinations."

These three contraindications to transperitoneal section constitute the above proposed definition for potentially infected cases. This group

1. Cannot be sectioned through the peritoneum, as Dieckmann states, and we thoroughly believe, without incurring more than minimal mortality.

2. Some cannot be delivered vaginally without inordinate prolongation of labor and heightened fetal risk.

3. All certainly should not be subjected to cesarean-hysterectomy.

We believe that those not susceptible to relatively facile and safe vaginal delivery, *should* be delivered by extraperitoneal section. We further believe that the application of extraperitoneal section to this group *constitutes its greatest value*. It is an important item in the obstetrician's armamentarium which increases the flexibility of his resource in best managing this, in our experience, very important group of cases.

How important is it? Schumann has indicated that any obstetrician of competence should be able to make so accurate a prognosis that hardly any case should disappoint predetermined possibilities of vaginal or abdominal delivery. In our clinic we are not so omniscient!

McKelvey more reasonably says: "Complete clinical and x-ray study will not separate pelvic dystocia problems into two absolute groups, one for certain spontaneous delivery, and another for section." "There is a doubtful range at the inlet, at mid-pelvis, and four or five . . . at the outlet." Not only is this statement true as regards clinical and x-ray study, but this "doubtful range" is broadened by the impossibility of accurate pre-estimation of the intangible functional factors concerned in labor. Perhaps we have been so intent on trying to improve prognostic resource by refinements in study of the configuration and size of the pelvis that we have too often forgotten that the woman in labor is something more than a skeleton. Prognosis entirely based on estimation of the resistances to successful delivery, which ignores the functional capacity of the woman, with special reference to her uterus and, to some extent, even her psyche, will lead to serious pitfalls and sad errors of judgment. This functional status cannot

tissues about the uterus at the time of the operation and I believe that the mortality without operation would have been close to 100 per cent. He had a 30 per cent mortality in his first 67 cases, 18 per cent in his next 17, and no deaths in the following six.

Dr. Cosgrove states that cesarean-hysterectomy is a formidable operation. Many doctors have this idea, and therefore do not perform this operation except in the absolutely necessary cases. Their operating time will therefore be slow, and there will be much spill.

What is most important, they may amputate too high, thereby defeating the purpose of the operation, which is to remove all of the uterus.

Dr. Cosgrove states that soiling of the peritoneum can be easily prevented with the extraperitoneal approach. This is an obvious fact, and it is for that reason I favor the extraperitoneal. Any hole in the peritoneum, protected only by catgut or even a nonabsorbable suture, is a weak point for leakage of infected material (lochia) into the peritoneal cavity. I do not believe the patients die from peritonitis as a result of the immediate soiling, but from the leakage through the incision or hole in the peritoneum. The fact that the authors have collected over 667 patients with 152 (23 per cent) perforations of the peritoneum with a very low mortality, does not prove the safety of the operation.

We have set up at the Chicago Lying-in Hospital certain contraindications against the low cervical cesarean section because our experience and the experience of others indicate that if one oversteps these, the morbidity and mortality are markedly increased. These are as follows: (1) labor and/or ruptured membranes over twenty-four hours, (2) attempts at delivery by forceps or version, (3) induction of labor by bag, bougie, or pack, (4) evidence of uterine infection, (5) repeated rectal or vaginal examinations, and (6) a dead or damaged fetus.

We have undoubtedly performed a number of unnecessary sections, but the fact that we have had only nine deaths (five from infection) in over 2,000 cesarean sections, speaks well for our safeguards. I have performed cesarean section with no maternal mortality on a number of occasions after each contraindication listed above; but I had been in personal charge of the entire labor. I think the time interval between intrauterine manipulation and the operation is important.

*Indications for craniotomy or cesarean-hysterectomy.*—(1) A bag, bougie, or pack has been in the uterus for twelve to twenty-four hours or longer, (2) labor for twelve or more hours after attempts at delivery, (3) foul-smelling amniotic fluid, (4) repeated vaginal examinations with hands or unsterile gloves, and (5) labor of thirty-six to forty-eight hours or more associated with: (a) temperature of 38.5° C. or more, (b) chills, (c) positive blood culture, (d) pathogenic organisms in the amniotic fluid in large numbers and associated with (a), (b), or (c). (6) More than twelve rectal or six vaginal examinations.

The mere statements by various authors that the patients treated by extraperitoneal section were infected is very doubtful evidence. I question the need for the extraperitoneal type in all of the 250 cases reported by Waters, since 140 were presumably clean cases and only 90 had preoperative morbidity or sepsis. Sixty had positive uterine cultures. Preoperative fever is no absolute criterion for infection, nor are the positive uterine cultures, even though 56 showed pathogenic organisms.

Several years ago, Adair and Ira Brown reported our results in taking cultures at cesarean section. It is worth noting that 28 per cent of the cultures were positive before and after opening the peritoneum, but 64 per cent were positive before closing the peritoneum. I do not know when Waters took his cultures. I would be more impressed if they were taken before the baby was delivered and if some attempt were made to determine the number of bacteria.

We have performed six sections according to Waters' technique. None were indicated, but the last one had a septic course. The patient had been in labor only twenty-four hours and recovered without other complications, but the baby died within twenty-four hours from pneumonia.

Dr. Cosgrove reports 483 extraperitoneal sections with six maternal deaths, a rate of 1.24 per cent. Five of the deaths were from infection. Since most of these operations were performed in potentially infected patients (whom we would have delivered vaginally or by

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88 CLIFTON PLACE

39 GIFFORD AVENUE

## Discussion

DR. W. J. DIECKMANN.—The extraperitoneal cesarean section is theoretically ideal for all patients where it can be performed. I agree with Dr. Cosgrove that it is much safer than the laparotrachelotomy in potentially infected patients. I do not believe it is as safe in infected patients as vaginal delivery or cesarean-hysterectomy. The latter operation, in my opinion, is *the safest treatment for infected patients*. Extraperitoneal cesarean section should be performed only by the experienced obstetrician who has a sufficient number of clean patients requiring cesarean on whom he can learn the technique. The occasional operator should not attempt the extraperitoneal or, in fact, any type of cesarean section.

Dr. Cosgrove states that craniotomy on a living fetus is abhorrent and that it should be considered wholly obsolete and outlawed. I do not agree with him because after a patient has been in labor for twenty-four to thirty-six or more hours, the number of stillbirths increases steadily, and many fetuses do not survive, even if delivered by cesarean section. Some who do survive show evidence of intracranial injury and are better off dead.

Dr. Cosgrove questions our mortality of 1.0 per cent for cesarean-hysterectomy. He is correct. This figure is weighted by many hysterectomies on clean patients. We are now trying to determine just what our mortality is in cesarean-hysterectomy for the treatment of infected patients.

For many years, I have felt better after a cesarean-hysterectomy than after any type of cesarean section. The postpartum uterus is an excellent culture tube because of its poor blood supply, and I believe that many women would be alive today had the uterus been removed at cesarean section or very early in the septic puerperium.

I stated in a recent paper that Baldwin's results in the treatment of puerperal infection by hysterectomy proved conclusively that cesarean-hysterectomy was a safer operation than the extraperitoneal section. Cosgrove questions the validity of this statement because Baldwin had a mortality of 26 per cent, and their mortality in extraperitoneal section was only 0.8 per cent. Of Baldwin's patients 77 per cent had pus in the uterine wall or in the



cesarean section is necessary for any reason, we would prefer the low cervical section, since the statistics in our series at the present time seems slightly to favor this operation.

The question has been raised of the need to sacrifice the living baby by delivery per vaginam in cases of outspoken sepsis. At the time this decision is made, it must be remembered that not all of these babies will survive if delivered by cesarean section, in fact, many of them have been infected secondarily to an ascending placentitis long before the decision to operate is made. These will be found to have a septicemia at birth from which many do not recover. I certainly would not hesitate to sacrifice a fetus which I thought had very little chance of survival in order that I might increase the chances for the survival of an infected mother by delivery from below. In the overwhelming majority of such cases we have been able to deliver after craniotomy without significant subsequent gynecologic pathology.

Recently we have put all such patients on sulfonamides and penicillin prophylactically. As soon as the membranes ruptured we have been able to demonstrate sulfonamides in the amniotic fluid and blood of the infant. While we do not have comparative figures, we are of the opinion clinically that we have reduced our fetal mortality and morbidity by this means.

I would like to ask Dr. Cosgrove what his statistics show as regards fetal salvage in those cases in whom a frank infection was present at the time of operation.

Another question which frequently is brought up in connection with the discussion of these operations is the number of bladder injuries which have to be repaired during the operation, and of this number what per cent developed vesicovaginal fistula, and of this group what per cent have to be closed surgically.

DR. JAMES E. FITZGERALD.—I would like to ask Dr. Cosgrove whether he has delivered any of these patients from below after they have had the operation described.

DR. LOUIS RUDOLPH.—I would like to ask Dr. Cosgrove what is his test of labor.

DR. STUART ABEL.—How much technical difficulty is encountered in attempting extraperitoneal section after a previous cesarean section?

DR. W. C. DANFORTH.—I would like to ask whether there have been deliveries from below after extraperitoneal section, and whether the incidence of rupture of the uterus is greater or less than it is after low cervical section.

DR. A. F. LASH.—I would like to ask Dr. Cosgrove whether they have employed the Hillis impression method. We find it of great help here in determining whether we have disproportion in borderline cases.

DR. COSGROVE (Closing).—I have, I think, accomplished my purpose in coming here tonight if I have been able to impress upon you that the whole discussion of extraperitoneal section as opposed to the Porro operation is not limited to the actually severe infected cases. My chief point is the applicability of extraperitoneal cesarean section to a group potentially infected which Dr. Dieckmann and I agree should not be subjected to the transperitoneal operation.

Dr. Falls' discussion of the relative safety of the classical section and the lower segment section is most interesting. He has pointed out that he prefers doing a lower segment operation because of the lessened mortality.

Dr. Dieckmann has made reference to the sleepless nights we used to have after doing cesarean section. The expectation was that we should have two or three days' hard struggle before we were sure the patients were safe. The reason for the change is better preparation and better anesthesia and not altogether the shift to the lower section operation.

Bladder injuries have not been very frequent. We reported fatal results of bladder injury in one of our cases. I recall another in which I severed the ureter in doing a Latzko, but I was able to repair it. Bladder injuries are more apt to attend the Latzko type of operation and, when they do occur, they are somewhat difficult to repair. These patients

cesarean-hysterectomy) and some in infected patients, the low mortality demonstrates the increased safety of the operation over that of the transperitoneal low cervical.

I am pleased to note that Dr. Cosgrove and Dr. Waters are stressing the value of the extraperitoneal section in *potentially* and not actually infected cases. This distinction is important because the reputation of the Margaret Hague Hospital and its staff will stimulate many doctors to practice the Waters' operation in unsuitable cases. The results would be an increasing mortality from section instead of a decreasing.

My own experience, as well as all the available evidence, demonstrates beyond question that the infected patient should be delivered vaginally if it can be done without too much trauma, otherwise, by cesarean-hysterectomy. In the latter operation the entire corpus must be removed, spill must be kept at a minimum, adequate drainage provided through the cervix and vagina, and a peritonitis routine instituted for forty-eight hours or more post-operatively. If sulfonamides and penicillin are administered prophylactically, the dosages must be large and the urine volume maintained at 1,400 c.c. per twenty-four hours.

DR. FREDERICK H. FALLS.—When I was asked to discuss this paper my first inclination was to refuse because of a very limited experience with the extraperitoneal operation. The reason for this lack of experience is that we have been busy in our clinic with a different problem in cesarean sections, namely, to determine whether the low cervical or classical operation is the better operation. We have been doing every other case by the low cervical method since 1930. We have felt that it may be of interest to discuss Dr. Cosgrove's paper from a negative angle, that is, what happens if you do cesarean section and do not use the extraperitoneal method.

We have had approximately 20,000 cases and, of these cases, 285 have been delivered by cesarean section. Among these, six deaths occurred, a mortality of 2.1 per cent. Of these, two were due to peritonitis following operation, which gives a mortality rate of 0.7 per cent for this complication. Of the 285 cases, 122 were classical cesarean sections in which there were two deaths; 142 were low cervical cesarean section in which there were no deaths. Twenty-one were Porro cesarean sections in which there was one death attributed to pre- and postoperative hemorrhage from a ruptured uterus.

We do not share Dr. Cosgrove's fear of the classical cesarean section resulting in peritonitis and death, since we lost only two patients from peritonitis in this group, and one of these had a serious toxemia which may well have been the deciding factor in producing the infection. These were all done without the use of sulfonamides in the wound, or taken by mouth, or intravenously administered before or after operation.

In 142 low cervical sections in which no deaths occurred, there were no exceptions made for potentially infected cases. Twenty-one so-called Porro operations were done, only two of which were considered necessary because of the presence of actual infection. One had a carcinoma of the rectum with rectovaginal fistula, and the other a long labor with a long period of ruptured membranes with infection present. Both of these mothers survived the operation, as did their babies. The remainder of the Porro operations were done for various reasons, such as ruptured uterus, premature detachment of the placenta, fibroids, and such complications. We do not feel that this operation must be reserved for seriously ill patients any more than that the extraperitoneal operation must be so restricted. It may be done in patients running a low grade temperature in which it is feared an active infection is present. It may be done for an intercurrent infection such as a pneumonia, typhoid, appendicitis, and I have even done one case successfully in a patient with erysipelas of the face, toxemia of pregnancy and subacute gonorrhea. Technically, the operation is not difficult. It can be done under local anesthesia and the shock is very little, if any, greater than that of an uncomplicated cesarean section. If done before the patient is allowed to become a poor risk because of procrastination on the part of the obstetrician. The advantage of this procedure is that it removes the possibility of the patient developing a fatal puerperal sepsis, since there is no uterus to become infected.

We hardly agree with Dr. Cosgrove in adopting a conservative attitude in labors of twenty-four and thirty-six hours, and feel that in the absence of demonstrable infection, if

## A DISCUSSION OF PELVIC VARIATION AND A REPORT ON THE FINDINGS IN 100 NEGRO WOMEN\*

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FROM time to time the author and his associates have reported on the architecture of the bony pelvis in various groups of our population as it is revealed by roentgen investigation. The more recent of these communications include: "A Study of Pelvic Type in 582 Primigravid White Women, 104 Student Nurses, and 107 Young Girls," in 1939<sup>1</sup>; "An X-ray Study of the Pelvis in 69 Adult White Males," in 1939<sup>2</sup>; "A Comparative Study of the Male and Female Pelvis," in 1940<sup>3</sup>; "A Clinical Study of Roentgen Pelvimetry in 1,100 White Women," in 1941<sup>4</sup>; "A Clinical Study of the Pelvic Midplane in 153 White Women," in 1944; and "A Study of the Growth and Development of the Pelvis in 107 Individual Girls Before, During, and After Puberty," in 1944.<sup>5</sup> The present study adds to this group findings in 100 adult Negro women delivered of their first full-term child on the wards of the New Haven Hospital. As in previous clinical studies, these cases represent a consecutive series, except that in the present instance the sequence is broken into two groups of 71 and 29 respectively by an interval of several months during the war.

Before analyzing these latter findings, it may prove useful to review some conclusions with regard to pelvic architecture and its relation to clinical obstetrics. The shape of the pelvic inlet in early childhood is characteristically elongated anteroposteriorly, or *dolichopellic*, and, if a pelvis of this type were to grow symmetrically, it would have a similar shape in adult life. From this it would appear that the round or flattened forms of the adult pelvic inlet may arise as a result of either of two mechanisms; an excessive growth laterally, that is of the transverse diameter, or a diminished growth anteroposteriorly. From the studies cited above, it seems apparent that the lessening or incomplete development of the anteroposterior diameter is the more important mechanism, increasingly so as the degree of flattening becomes more extreme.

For purposes of classification we may say that the tendency of a pelvis to retain most of the relationships of fetal and childhood conformation, and thus remain relatively elongated anteroposteriorly may be spoken of as *dolichopellism* (*dolicho* = long); while the tendency in a pelvis to become broadened transversely and short anteroposteriorly is that toward *platypellism* (*platy* = broad or flat). A simple and useful classification of pelves, therefore, can be based upon these anteroposterior and transverse pelvic relationships, as suggested by William Turner in 1885.<sup>6</sup> The relative size of these two dimensions is most conveniently expressed as the pelvic index. This index is the anteroposterior diameter of the pelvic inlet times 100, divided by its maximum

\*This study was made possible through grants from the Clinical Research and Teaching Funds of the Yale University School of Medicine.

had no persistent fistula, nor did they require subsequent surgery to repair the results of bladder injury. In the supravaginal type of injury of the bladder it is very handy to repair it without leaving any fistula. These injuries are easily recognized.

We have had a few spontaneous deliveries after extraperitoneal section. I have no statistics as to the number. We have just this week reoperated upon a patient who had had a Latzko several years ago. I did a low transverse operation, and it was remarkable how simply the bladder separated from the uterus. There was not the slightest technical difficulty in the usual approach to the lower segment.

What is our test of labor? The test of labor is continued in our hands so long as the patient is making actual progress in labor commensurate with the best estimation we can make of the efficacy of uterine activity. We do not put any time limit on it. That, of course, places the decision on the judgment of the operator or observers.

The technical difficulty of this extraperitoneal section after previous cesarean section I do not think has been tested in our hands, because if a woman has a history of previous section for cephalopelvic disproportion, she will hardly be subjected to so long a test of labor as to require resort to the extraperitoneal type. I do not recall an instance of resort to an extraperitoneal operation in a patient who had had a previous cesarean section because of cephalopelvic disproportion.

Rupture of the uterus we have not seen following extraperitoneal cesarean section, nor have we seen massive calamitous rupture of the uterus after any lower segment operation. That brings up the question, what is meant by rupture of the uterus? Is it simply solution of continuity of the wall of the uterus? Then we have had rupture following lower segment operation, in that we have had incompletely healed primary incisions, sometimes with the membranes shining through, constituting a solution of continuity of the myometrium. We have never had an extensive "blowing-out" rupture, with extrusion of the fetus in any type of lower segment operation.

We make extensive use of the Hillis impression method and value it highly.

probably too much attention to the classification of the pelvis by its shape. Accepting the fact that the lengths of the pelvic diameters, in common with other anatomical measurements, are normally distributed, we may from the given

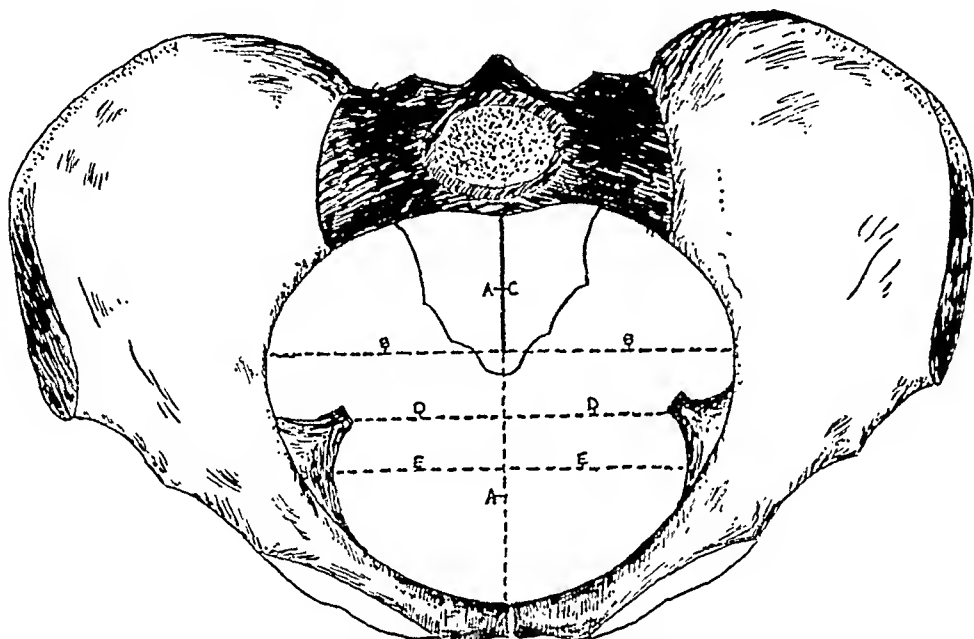


Fig. 1.—The pelvis seen from above. *A*, Anteroposterior diameter of inlet; *B*, transverse diameter of inlet; *C*, posterior sagittal diameter of inlet; *D*, interspinous or transverse diameter of midplane; *E*, widest transverse diameter of outlet.

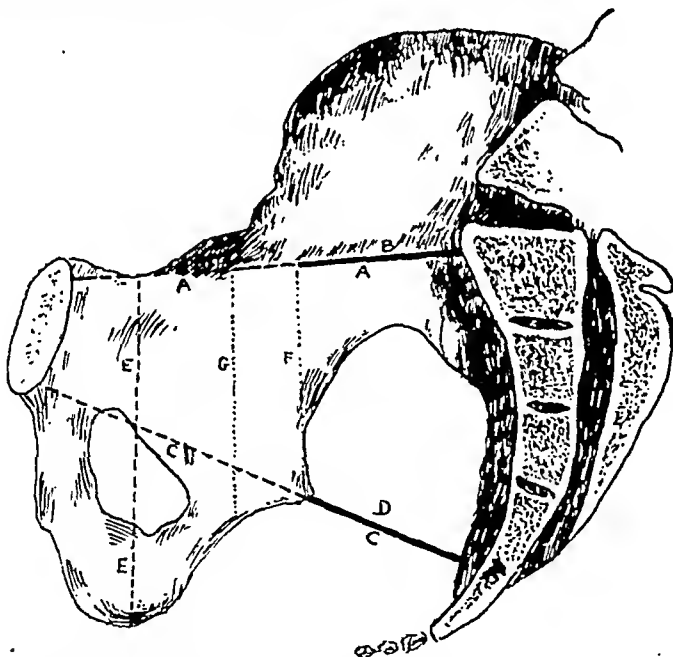


Fig. 2.—Lateral aspect of pelvis. *A*, Anteroposterior diameter of inlet; *B*, posterior sagittal diameter of inlet; *C*, anteroposterior diameter of midplane; *D*, posterior sagittal diameter of midplane.

figures calculate the corresponding figures for the pelvic index which, after all, is the chief guide to the shape of the pelvis."

The following diameters of the pelvis we have found to be clinically useful and have been used throughout most of the studies referred to here. Figs. 1 and 2.

transverse diameter. By means of this index, it is possible to group together pelves which show the same degree of anteroposterior flattening or elongation, regardless of their absolute size. Turner classified pelves into three types on the basis of their pelvic index. Those with an index of 95 or more he called dolichopellic, those with an index from 90 to 94.9 mesatipellic, and those with an index less than 90 he termed platypellic. For anthropologic purposes, the use of the pelvic index is ideal and would be useful in clinical obstetrics, except that it is a little unwieldy because it cannot always be estimated by simply viewing dimensions.

A simpler and useful device for classifying pelves based upon the principle of the pelvic index follows. In this method pelves are divided into four general groups:

1. *Dolichopellic Type*.—The anteroposterior diameter of the inlet is longer than the transverse.

2. *Mesatipellic Type*.—The anteroposterior and transverse diameters of the inlet are equal or the transverse diameter is no more than 1 cm. longer than the anteroposterior.

3. *Brachypellic Type*.—The transverse diameter is more than 1 cm. and less than 3 cm. longer than the anteroposterior diameter.

4. *Platypellic Type*.—The transverse diameter is 3 cm., or more than the anteroposterior diameter.

We have found this method of pelvic classification clinically useful as a ready means of identifying pelves for purposes of description and record. To complete the survey certain morphologic characteristics, not associated with mensuration, may be added to the pelvic survey, such as the wideness or narrowness of the pelvic forepart, sacrosciatic notch, etc.

From our investigations of adult pelves in both sexes, it appears that at the present time methods of classification based on sex characters may be confusing and, in some instances, not altogether sound. This is in view of the fact that our studies in male pelves show essentially the same variations that we find in the female. Thus, in the investigation of Gruelich and the author<sup>2</sup> we state, "our findings indicate that the pelvic inlet of the male is as variable in shape as that of the female. . . . It is evident, therefore, that there is in our population at least no one type of male pelvis, just as there is no one type of female pelvis." And again, "It is evident from the tracings that the shape of the pelvic inlet of most of the men of our series is quite different from that described in the textbooks as typically masculine. Indeed, the pelvic inlet of some of our males so closely resemble that of some of the student nurses of our earlier series that it would be difficult in certain cases to determine the sex of the individual from the shape of the pelvic inlet alone."

It seems clear that, while certain sex characteristics of male and female pelves can be accepted as more or less constant, others formerly thought to be constant are highly questionable. In addition, "normal" variations in anteroposterior and transverse relationships are apparently present in both sexes in wide distribution. That the anteroposterior and transverse relationships can form a suitable basis for clinical classification has been recently re-emphasized by C. Nicholson,<sup>7</sup> who states: "Obstetricians have of late devoted a great deal,

TABLE IV. AVERAGE DIAMETERS

	DOLICHOPELLIC	MESATIPPELLIC	BRACHYPELLIC	PLATYPELLIC
<i>Inlet</i>				
Anteroposterior	12.36	11.28	10.70	9.23
Transverse	11.50	11.79	12.46	12.76
Posterior sagittal	4.50	4.03	4.08	2.33
<i>Midplane</i>				
Anteroposterior	12.54	12.31	12.45	12.16
Transverse	10.09	10.24	10.84	11.50
Posterior sagittal	4.94	4.79	5.00	4.63
<i>Outlet</i>				
Widest transverse	11.38	11.50	12.00	12.40

TABLE V

Less than 90	(Platypellie)	26
90 to 94.9	(Mesatipellie)	21
95 or more	(Dolichopellie)	53

TABLE VI

New England States	38
Middle Atlantic States	4
Southern States	49
Missouri	1
West Indies	7
Portugal	1

TABLE VII

	SPONTANEOUS BIRTH OR LOW FORCEPS	OPERATIVE BIRTH
Dolichopellie type	26	3 (2 forceps for pelvic indication)
Mesatipellie type	39	4 (2 forceps for pelvic indication)
Brachypellie type	22	3 (3 cesarean sections for pelvic indications)
Platypellie type	1	2 (2 cesarean sections for pelvic indications)
<i>Operative Incidence for Pelvic Indications</i>		
Dolichopellie		6.8 per cent
Mesatipellie		4.6 per cent
Brachypellie		12.0 per cent
Platypellie		66.6 per cent

Information as to the birthplace of these women was recorded, but no correlation between pelvic type and such geographical distribution was noticed. The range is recorded in Table VI.

As in the previous studies, the clinical course of labor was reviewed according to pelvic type and summarized in Table VII.

The series is too small for definitive clinical evaluation, but the evidence presented bears out findings previously seen in a much larger group of white women; that is, that the round (mesatipellie) or elongated (dolichopellie) pelvis is more favorable for natural birth than the oval (brachypellie) or the flat (platypellie) pelvis.

At first thought it would appear that the increased incidence of the dolichopellie type in these Negro women over the white group might be explained as the result of racial influence; however, a study by Gruelich and the author<sup>8</sup> in 100 white women in a more privileged economical group than the 500 white ward patients cited above showed an even greater tendency toward dolichopellism than the Negro group. These findings are recorded in Table VIII.

### Pelvic Inlet

*Anteroposterior Diameter.*—A line drawn from the upper posterior surface of the symphysis to the sacrum at a point where the iliopectineal lines would converge if they were to be extended.

*Transverse Diameter.*—The widest transverse diameter of the pelvic inlet.

*Posterior Sagittal Diameter.*—That part of the anteroposterior diameter which lies posterior to its intersection by the transverse diameter.

### Pelvic Midplane

*Anteroposterior Diameter.*—A line drawn from the lower posterior surface of the symphysis pubis posteriorly through the level of the ischial spines to the lower sacrum.

*Transverse Diameter.*—The shortest diameter between the ischial spines.

*Posterior Sagittal Diameter.*—That part of the anteroposterior diameter which lies posterior to its intersection by the transverse diameter.

### Outlet

*Widest Transverse Diameter of the Outlet.*—A line drawn between the ischial bones at the base of the ischial spines.

(All of the above are determined roentgenologically.)

The pelvic survey of the outlet also includes the bituberal diameter as determined manually. This is not included in the present and previous studies.

For purposes of evaluating the present study, a summary of the findings on 500 white primigravid women are given<sup>4</sup> in Table I.

TABLE I. TYPE DISTRIBUTION

Dolichopellic type	113	or 22.6 per cent
Mesatipellic type	233	or 46.6 per cent
Brachypellic type	144	or 28.8 per cent
Platypellic type	10	or 2.0 per cent

TABLE II. AVERAGE DIAMETER RANGE IN 500 PELVES OF WHITE WOMEN

	DOLICHOPELLIC	MESATEPELLIC	BRACHYPELLIC
<i>Inlet</i>			
Anteroposterior	12.0 to 13.0	11.5 to 12.25	10.5 to 11.5
Transverse	11.5 to 12.25	12.0 to 12.75	12.25 to 13.25
Posterior sagittal	4.5 to 5.5	4.25 to 5.0	4.0 to 4.5
<i>Midplane</i>			
Anteroposterior	12.0 to 13.0	11.75 to 13.0	11.5 to 12.75
Transverse	9.25 to 10.25	10.0 to 10.75	10.0 to 11.0
Posterior sagittal	4.75 to 5.5	4.5 to 5.5	4.5 to 5.5
<i>Outlet</i>			
Widest transverse	11.3	11.9	12.0

The pelvic type distribution of the present study of 100 primigravid Negro women is shown in Table III.

TABLE III

Dolichopellic type	29	or 29.0 per cent
Mesatipellic type	43	or 43.0 per cent
Brachypellic type	25	or 25.0 per cent
Platypellic type	3	or 3.0 per cent

To those interested in the pelvic index, as described by Turner, in these 100 Negro pelves, Table V shows the distribution.



favorably influenced by nutrition. Clinical experience has shown that pelvic development toward dolichopellism and not toward platypellism is desirable from the obstetric point of view.

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TABLE VIII

Dolichopellic type	37.0 per cent
Mesatipellic type	46.0 per cent
Brachypellic type	17.0 per cent
Platypellic type	0.0 per cent

### Comment

Variations of the pelvis as they occur in the adult female offer considerable speculation as to etiology. Undoubtedly numerous factors contribute, among which those having to do with nutrition seem to be of prime importance. In 1936 the author discussed the question, "Is the oval or female type pelvis a rachitic manifestation?"<sup>9</sup> pointing out that in the oval, or so-called "female" (brachypellic) type pelvis the iliac portion of the line of terminal length is consistently shortened. The association of relative shortening of this sector with rachitis was emphasized by Breus and Kolisko in 1904.<sup>10</sup> This study concluded with the observation, "From available information concerning pelves in aboriginal people living in climates where rachitis does not occur, it appears evident that the round type pelvis is greatly predominant. Furthermore, it seems apparent that the unusual incidence of the round (mesatipellic) and anthropoid (dolichopellic) types in the women of our population must be explained on grounds other than those based on such influences as race and constitution." In 1939, in "A Study of Pelvic Type"<sup>11</sup> by Greulich, Thoms, and Twaddle, in a comparison of body build with pelvic type, it was stated, "The high incidence of long oval (dolichopellic) and of round (mesatipellic) pelves among the largest women of both groups suggests the possibility that nutritive and other factors which make for the attainment of maximum normal growth tend to prevent that degree of anteroposterior flattening of the pelvis which has come to be regarded as characteristically feminine."

More recently, other observers have emphasized the importance of the role of nutrition in the ultimate shape of the pelvis. Allen's recent (1944) New Zealand study<sup>11</sup> of 214 cases showed 54.2 per cent of dolichopellic pelves (index over 95). He concludes, "... that the shape of the pelvis is determined more by environment and diet than by inherited racial tendencies." Nicholson, referred to previously, also states, "The length of the conjugate diameter is very considerably influenced by nutrition, and, in the absence of any large population which up to now can be considered as fully nourished in childhood, it is still quite impossible to determine the mean to which the measurement tends." In summarizing his series of measurements of the adult female pelvis, Nicholson states, "Pelvimetry by radiology in 640 cases is analyzed to show that the length of the conjugate diameter of the female pelvis is very sensitive to nutrition, and the figure quoted in textbooks of anatomy for this diameter is too low."

### Conclusion

Evidence has been given which shows that the adult female pelvis in the white and black races is subject to considerable variation and that the tendency for the adult pelvis to maintain its fetal and childhood general relationships is

### Roentgen Mensuration

It was felt that a study of the actual measurements of the various pelvic planes might be of value in indicating significant dystocia warnings. Most obstetricians are familiar with normal and abnormal inlet measurements, but the significance of contractions at lower levels and the influence of lower sacral variations, side wall convergence, prominent spine, and narrow subpubic angles must be re-evaluated, since these factors can be more accurately measured by roentgen pelvimetry than by the older method of routine external pelvimetry of the outlet. It was obvious from the beginning of the study that, with the elimination of rickets, osteomalacia, and chondrodystrophy from our clinical material, absolute contraction of the pelvic inlet with true conjugates of 7.5 cm. or less were very rarely seen, and most of the cases were relative or borderline pelvic contractions. In an attempt to offer a prognosis in these difficult cases, it was decided that the sum of the anteroposterior and transverse diameters at any given pelvic plane is a more reliable index than the separate consideration of each, because they mutually compensate for each other.

As far as pelvimetry is concerned, this principle of adding the transverse to the anteroposterior diameter is our chief criterion for estimating the prognosis.

A statistical review of pelvic measurements as obtained by our method of radiopelvimetry in correlation with the ultimate mode of delivery reveals the following:

1. Patients who delivered spontaneously or who required simple outlet forceps displayed pelves, the sum of whose true conjugate and transverse diameters of the inlet averaged 24.8 cm.; and the sum of whose interspinous and posterior sagittal diameters of the midpelvis averaged 15.7 centimeters. In addition, it was noted that only rarely did uncomplicated delivery occur from a pelvis, the sum of whose inlet diameters were lower than 22 cm., or from a pelvis, the sum of whose midpelvic diameters were lower than 14.0 centimeters. Below these figures either midforceps or cesarean section was usually performed.

2. Patients requiring midforceps operations displayed pelves, the sum of whose true conjugate and transverse diameters of the inlet averaged 24.4 cm., and the sum of whose interspinous and posterior sagittal diameters of the midpelvis averaged 14.9 centimeters. As might be expected, little difficulty was met during the process of engagement. However, descent of the head below the level of the interspinous diameter became increasingly difficult as the total of the midpelvic diameters decreased. It is to be noted that we used the total of the diameters of the midpelvis (interspinous and posterior sagittal) for prognosticating. Experience has proved that a relatively small interspinous diameter can be readily compensated for by a very ample posterior sagittal diameter. More specifically, we have found that a good prognosis for vaginal delivery could be given for pelves with interspinous diameters from 9 to 9.5 cm., provided the posterior sagittal diameter of the midpelvis is large enough to total 14 cm. or more when added to the interspinous diameter. Limitations, of course, on this general rule are imposed by other complicating conditions, such as malposition of the fetus, large babies, soft tissue dystocia, pelvic anomalies, etc. Delivery from below occurs only rarely with midpelvic dimensions totaling 13.5 cm. or less; and almost never in pelves whose midpelvic dimensions total

# THE VALUE AND LIMITATIONS OF PELVIORADIOGRAPHY IN THE MANAGEMENT OF DYSTOCIA, WITH SPECIAL REFERENCE TO MIDPELVIC CAPACITY

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THE occasional untoward outcome of a pregnancy, resulting from following the radiological criteria in managing a case of dystocia, has led some to discredit the entire procedure of pelvioradiography.

In the great majority of cases, the obstetric prognosis and treatment suggested by the x-ray study of the pelvic measurements and architecture, combined with an evaluation of fetal pelvic relationships, is of great value in the management of dystocia. However, in approximately 2 per cent of the cases in which dystocia is anticipated or appears unexpectedly during labor, the radiological advice given and followed led to an undesirable outcome, and subjects the radiologist or obstetrician reading the films to unfavorable criticism. Usually no allowance is made for any lack of skill or mistakes in clinical judgment on the part of the operator, but the x-ray department is blamed.

In order to determine whether this disparaging attitude is justified, we felt that a comprehensive study of the limitations, as well as the value of pelvioradiography should be made. Our material consists of five hundred consecutive cases referred to the x-ray department because of dystocia, either actual or feared. These cases were studied with particular reference to the evaluation of midpelvic contraction in dystocia.

## Roentgen Pelvimetry

A comparison of techniques of roentgen pelvimetry was made by measuring the same patients by various methods. We utilized four well-known methods for each of one hundred patients. The pelvic diameters obtained by the precision stereoscopic method, the Thoms-Torpin isometric scale, and the Snow ruler and Ball nomogram gave results that in all cases were within 0.1 cm. of each other.

We therefore felt that the particular technique used is of less importance than a wide experience in its use. We still use our own combined technique of studying the pelvic architecture by the precision stereoscope, and measuring the diameters with the Snow ruler checked by the isometric scale. A series of measurements on detached and articulated skeletal material showed our results to be accurate to within 0.1 cm. when compared to measurements of the actual material. We are, therefore, convinced that the technique of roentgen pelvimetry used in this study is reliable.

pelvic diameter, the postsagittal of the midpelvis. In many cases, a narrow interspinous diameter is compensated for by an over-ample postsagittal diameter, especially if the other factors (lateral bore, side walls, etc.) are adequate. The pelvic outlet is not very important from an obstetric standpoint, if it is not confused with the midpelvis. The diameters concerned in the outlet are the bituberous and posterior sagittal, which are always greater than the corresponding midpelvic measurements.

### Cephalometry

We have found that our measurement for the circumference of the head is accurate to within 1.0 cm. when checked with the circumference obtained at birth. Knowing the circumference, we employ the Ball nomogram for determining head volume.

*Fetometry.*—Attempts were made at predicting the weight of a fetus from the circumference of the head. One-fourth of the cases differed by more than one pound, and therefore were of no value. Since only three-fourths of our cases showed a definite correlation between the size of the head (circumference or volume) and the weight of the baby, we feel that, in any individual case, the judging of weight from volume cannot be relied upon.

The failure of predicting weight on the basis of the x-ray measured circumference of the skull is not due to any fault of roentgen technique. The fallacy lies in the infant itself. Two infants, both with the same size head, can differ from each other by 3 to 4 pounds, because of difference in length, and muscular and fatty development. On one occasion, two infants having the same skull circumference by x-ray weighed 5 and 9 pounds, respectively. The children were then measured in the crib and both found to have the same skull circumference, yet one was almost twice as heavy as the other.

A number of children (200) were measured in the nursery and, while the average weight increased with the increase in skull circumference, the extremes in each group differed from each other to such an extent that in the individual cases the procedure was unreliable because of the overlapping (Table I).

TABLE I.

CIRCUMFERENCE	AVERAGE WEIGHT	LIGHTEST	HEAVIEST
33-34 cm.	6 lb. 2 oz.	5 lb. 5 oz.	7 lb. 13 oz.
34-35 cm.	7 lb.	4 lb. 8 oz.	9 lb. 14 oz.
35-36 cm.	7 lb. 3 oz.	5 lb. 13 oz.	8 lb. 12 oz.
36-37 cm.	8 lb.	7 lb. 10 oz.	10 lb. 12 oz.

### Pelvic Architecture

All pelves were classified according to their architectural features into the pelvic types of Caldwell, Moloy, and D'Esopo: gynecoid, android, anthropoid, and platypelloid. The android and platypelloid pelves were frequently given a poor prognosis, and operative deliveries were common in these groups. In the absence of disproportion, a favorable prognosis was usually given in the anthropoid and gynecoid types and operative deliveries were infrequent in these cases.

less than 13 centimeters. Under the latter conditions only premature and small fetuses can be delivered from below.

3. Patients who required cesarean section displayed pelves, the sum of whose true conjugate and transverse diameters of the inlet averaged 23.3 cm., and the sum of whose interspinous and posterior sagittal diameters of the midpelvis average 15.0 centimeters. These figures illustrate a definite reduction in inlet dimensions, though they exhibit fair to good midpelvic measurements. As might be expected in these cases, the main difficulty occurred during the process of engagement. Failure of the head to engage after a trial of labor usually led to the choice of cesarean section. However, since experience has shown that spontaneous delivery occasionally does occur from below in pelves whose inlet dimensions total from 22 to 24 cm., in such instances a test of labor is advised. Still more rarely is delivery from below seen to occur in pelves whose dimensions total from 20 to 22 cm., hence a short trial of labor to see if engagements will occur is suggested. With measurements below 20 cm., experience has shown that attempts at vaginal delivery of all but a very premature fetus are disastrous. More frequently than not, it has been seen that once engagement occurs in pelves of a borderline inlet, little difficulty is encountered while passing through the midpelvis.

*Summary.*—If the inlet measurements are below 23 cm. and/or outlet measurements below 14 cm., dystocia is expected. For inlet dystocia the prognosis is guarded or poor, with a section to be considered. For outlet dystocia the prognosis is usually a forceps operation. We do not recommend section for outlet dystocia alone unless it is combined with other unfavorable factors: android pelves, narrow outlet, prominent spines, converging side walls and lateral bore, and malposition, indicating that a forceps operation may be unduly difficult.

### Estimation of Midpelvis and Pelvic Outlet

The method of determining midpelvic volume by means of the interspinous measurements alone, as suggested by Ball, has not proved reliable in our hands in any individual case. The basic fault lies in the fact that the actual midpelvis, unlike the inlet, is irregularly circumscribed, and therefore cannot be accurately represented by any one volumetric figure. If the interspinous diameter alone is used to determine outlet volume, results may sometimes be apparently incongruous. For example, in our series there were six cases in which the "outlet volume" was 300 to 400 c.c. smaller than the volume of the head. Although two of these cases came to section, all of the other four delivered normal-sized infants spontaneously or with low forceps. Conversely, there were many cases in which the outlet volume measured greater than the volume of the head, but where midforceps was necessary because of midpelvic arrest.

We feel, therefore, that the present method of determining midpelvic volume by means of the interspinous diameter is inadequate, and may actually be deceiving. In giving a prognosis regarding the midpelvis or outlet, we place much greater emphasis on such factors as lateral bore, side walls, subpubic angle, and sacrosciatic notch. The interspinous diameter is, of course, of greater importance as well; however, we prefer to consider it in relation to the other mid-

miparas. Cesarean section was advised by us on five other cases, and all five terminated in section. However, whether these could have been delivered from below will remain an unsettled question, since section was performed on all early in labor. Only one case terminated in craniotomy. However, this mother had eclampsia and the fetus died in utero several hours before delivery. The average of the sums of the inlet diameters was 25 cm., and of the midpelvic diameters 15.4 cm., illustrating that breech presentation usually occurs in average-sized pelvis.

### The Value of Pelvioradiography in Dystocia

A total of 500 cases of suspected dystocia have been studied, and a radiologic prognosis given on the basis of pelvimetry, pelvic architecture, fetal pelvic relationships, and presentation. All cases were classified into one of four prognostic groups: good, fair, guarded, and poor, on the basis of criteria listed in Table II. A good deal of latitude is allowed in estimating the actual prognosis. For instance, a malpresentation, poor pelvic architecture, or asynclitism would induce us to place the prognosis one class below that which the actual pelvic measurements would indicate.

TABLE II. INLET PELVIMETRY AS A BASIS FOR PROGNOSIS

GROUP	PROGNOSIS	ANTERO-POSTERIOR	ANTERO-POSTERIOR PLUS TRANSVERSE	FETAL PELVIC RELATION	TREATMENT	OUTCOME EXPECTED
A	Good	Above 10.5 cm.	24 cm.	No disproportion	Labor	Spontaneous delivery is the rule
B	Fair	10-10.5 cm.	22-24 cm.	Borderline disproportion	Test labor	Vaginal delivery is usual
C	Guarded	9-10 cm.	20-22 cm.	Relative disproportion	Short trial labor	Cesarean section probable
D	Poor	7.5-9.0 cm.	Below 20 cm.	Absolute disproportion	Cesarean section	Cesarean section necessary

### Results

*Group A.*—(good prognosis) consists of those patients with no disproportion and a good prognosis.

Spontaneous delivery is the rule. There were 326 cases, or 65 per cent of the entire series in the group. In other words, almost two-thirds of the patients in whom dystocia was feared, the x-ray indicated a very favorable outcome with vaginal delivery. Considering that low forceps are often elective, it was decided to consider them as nonoperative and to judge all other forceps, operations, cesarean sections, and other vaginal maneuvers as operative. The number of patients that required operative deliveries in Group A was 52, and this amounted to 16 per cent of the group; the remaining 84 per cent delivered either spontaneously or with low forceps.

### Fetal Pelvic Relationship

Any floating head at term was requested to be x-rayed in the standing position to see if engagement would occur, and it very often did in cases where borderline disproportion existed, thus removing doubt and brightening the prognosis. If the vertex remained floating in the upright position the prognosis was better if it lay over the posterior segment of the inlet than over the symphysis, because we felt that the soft tissues of the pelvis directed the vertex into the pelvic axis more efficiently.

Asynclitism was always noted, and a posterior parietal presentation at the inlet was given a better prognosis than the anterior parietal presentation or Nägele's obliquity. At the midpelvis, an anterior parietal presentation was preferred.

Deflection attitudes of the vertex, such as face, brow, and extended occiputs made the prognosis more guarded. Occipitoposterior positions, except in the anthropoid pelvis, were considered unfavorable primary presentations. For the reasons previously given, the Ball volumetric comparison is not relied upon, but the fetal pelvic ratio was decided by studying the stereoscopic pictures of the inlet viewed through the precision stereoscope.

### Breech Presentations

In order to evaluate our skill in prognosticating breech presentations, a separate study was made of 50 cases. The determination of cephalopelvic compatibility where there is a breech presentation presents a more difficult problem in pelvioradiography. We have at present no accurate way of estimating the dimensions of the high floating head of the fetus. Our major criteria in prognosticating such deliveries have been: (1) pelvic dimensions, (2) pelvic architecture, and (3) fetal attitudes (deflection of the vertex, extended arms, and frank breeches). If the breech is extended, such as a frank breech, or if there are deflection attitudes of the vertex or extended arms, we are more likely to look for difficulty. It is difficult to estimate the size of a breech presentation; very little consideration is given to this factor unless the baby is obviously small and premature. The pelvic architecture is important if an extraction or forceps of the aftercoming head are to be performed. The decision, however, is based almost entirely on the pelvic measurements. A trial of labor in breech presentation is not practicable, and the decision for vaginal delivery or cesarean section is based almost entirely on the consideration of the pelvis. If it is average in size and of suitable architecture we advise vaginal delivery. On the other hand, if it is small or of poor architecture, section is advised. There is no middle ground to be covered by a trial of labor.

There are among our records a series of 50 pelvimetries with the fetus in the breech presentation. Forty-six were given a good prognosis for vaginal delivery. Forty-two of these did terminate with delivery from below with little or no difficulty; four terminated in cesarean section. However, not one of these four required section because of bony dystocia. One section was performed without a trial of labor, and three because of cervical dystocia in elderly pri-



1. *The Character of the Uterine Contractions of Labor.*—These will be mild and irregular, or painful but ineffectual, and nonphysiologic. Although the dystocia dystrophy syndrome is more common in the android pelvic type, it can occur in any patient.

2. *The Soft Tissue Factor.*—The greatest transverse diameter of the pelvic inlet, as measured in x-ray films, is reduced in the body by the psoas muscles by a variable but unknown amount. In highly muscular women of the short stocky variety, a considerable amount of available inlet space is eliminated by these muscles as they cross the pelvic brim. The estimation of the thickness of these muscles in the living person is impossible, and may lead to serious dystocia in relative disproportion cases. Small vaginas, congenital atresia and septa, and thick perineal muscles may obstruct labor even though the bony passage is ample. Dry labor or constriction ring dystocia may also upset the labor process.

3. *Behavior of the Cervix.*—Some cervices are long, thick, rigid, and do not seem to undergo effacement or dilatation as readily as others, resulting in so-called cervical dystocia.

4. *The Skill of the Obstetrician.*—That poor judgment and lack of skill are occasionally the cause of poor results in cases that were studied by pelvioradiography is obvious. The prognosis given is not adjusted to the ability of the operator, and a certain amount of error is thus admitted.

5. *The Age of the Patient.*—This factor is not considered in giving a radiological prognosis. In arriving at an obstetric prognosis, the physician must take this into consideration.

6. The previous history in multiparas is a reliable guide to obstetric prognosis, yet is not always available to the radiologist.

### Mortality

In this series of 500 cases of dystocia there were 25 stillbirths or neonatal deaths, an incidence of 5 per cent. This is slightly above the usual hospital figure, but is not very high for a dystocia series. Six of the babies died of conditions unrelated to delivery. Of the other 19 cases, cesarean section was advised in eight, but this advice was disregarded and difficult vaginal deliveries resulted in stillbirths. The other 11 were advised to have vaginal deliveries, but suffered the same fate. These are our 11 mistakes. There was no maternal mortality in this series.

### Summary and Conclusions

1. Provided that a reliable technique of roentgen pelvimetry is used, there is very little difference in the roentgen mensuration.

2. The sum of the anteroposterior and transverse diameters at any given pelvic plane is a more reliable index of pelvic capacity than the separate consideration of each.

3. If the inlet measurements total less than 23 cm. and/or the midpelvic measurements less than 14 cm., dystocia is expected.

4. Cephalometry and fetometry are too inaccurate to be of much importance in pelvioradiography.

5. The fetal-pelvic ratio was arbitrarily decided by the use of the precision stereoscope, and not by volumetric comparisons which were too often misleading.

There were 13 stillbirths, five of which died before delivery. The other eight died of intracranial hemorrhage, sustained during vaginal delivery. If these babies were delivered by section they probably would have survived; therefore we probably were wrong in eight instances in advising vaginal delivery.

The 12 patients sectioned in this group were sectioned for extrapelvic indications: we gave a correct prognosis of 98 per cent.

*Group B.*—(fair prognosis) includes patients with borderline disproportion and a fair prognosis. A test of labor is usually recommended, and vaginal delivery is the rule. There were 98 cases, or .20 per cent of the entire series, in this group. Operative delivery was necessary in 54 per cent. Midforceps was the most frequent operation, and was performed in almost one-third of the cases. The incidence of operative vaginal deliveries is much higher than in Group A, and a cesarean section had to be performed on 18 per cent of the patients. Cesarean section is often necessary in this group if the baby is over 9 pounds.

There were four stillborns in this group, two of which occurred before labor, and the remaining two during delivery. We achieved a correct prognosis in 98 per cent.

*Group C.*—(guarded prognosis) includes the group with a guarded prognosis because relative disproportion was evident, and a short trial of labor with early section was advised. Ten per cent of 49 cases were in this group. Forty-two patients, or 86 per cent, required operative deliveries. In 35 cases a cesarean section was performed. There were five stillborns in the 14 vaginal deliveries. One was a spontaneous premature stillbirth. The other four were due to delivery. In all four patients, a cesarean section was considered probable, and was advised after a very short trial of labor. In these four cases the advice was disregarded, and difficult vaginal delivery attempted after long labor. We made the correct prognosis in all of these cases, or 100 per cent.

*Group D.*—(poor prognosis) consists of those 27 patients, or 5 per cent of the series who had poor prognosis, absolute disproportion, and on whom an elective or immediate section was necessary. In 24 cases, a successful section was performed. In the three cases in which a vaginal delivery was attempted, stillbirths resulted.

In the entire series of 500 cases, a correct prognosis was given in 489 cases, or 97.8 per cent. A favorable prognosis was given in 326 cases, and 247 either delivered spontaneously or by low forceps, many of which were elective or prophylactic. Of the entire series, only 35 per cent required operative delivery; this indicates the conservative effect of pelvioradiography.

### The Limitations of Pelvioradiography

In our opinion, pelvioradiography is not as exact a science as geometry. Correct answers cannot always be given to a problem of dystocia from study of the x-ray alone. It is not a panacea for all difficult obstetrics, but it definitely takes its place with the ready availability of blood and plasma, chemotherapy, and improved methods of analgesia and anesthesia as one of the great advances in modern obstetrics. The limitations of value of pelvioradiography can be ascribed to the following conditions:

## HEART DISEASE IN PREGNANCY

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HEART disease long has been recognized as a serious complication of pregnancy. In recent years its increased prominence as a cause of maternal death has resulted, in part, from the improvement in prevention and treatment of other major causes of death, such as hemorrhage, toxemia, and infection. Patients with heart disease complicating pregnancy have always received careful study and treatment in the Woman's Clinic of the New York Hospital in an effort to lessen the immediate, as well as the future damage to the heart. Special attention has been directed to the disease, because its incidence has been found to be greater in the Northeastern States.

A five-year study of 418 patients with cardiac disease was made by Stander and Kuder<sup>1</sup> in 1937, and by Stander<sup>2</sup> in 1938. The present report deals in a similar fashion with the subsequent seven-year period, and embraces 720 additional cases. Thus a total of 1,138 women suffering from heart disease has been treated on the Obstetrical Service during the twelve-year period since Sept. 1, 1932. We have adhered to the New York Heart Association functional classification throughout, and shortly after the beginning of this second study period we adopted the revised classification as proposed by this association.

The 720 cases analyzed in the present study represent 3.02 per cent of the 23,858 pregnancies cared for during the period from September 1, 1937, through December 31, 1944. This incidence shows but a slight increase from that of 2.97 per cent in the previous five years. In the present series 425 of the patients were primiparas and 295 were multiparas.

TABLE I. FUNCTIONAL CLASSIFICATION OF CARDIAC DISEASE

TYPE	CASES	PER CENT OF TOTAL
Class I	227	38.48
Class II	322	44.72
Class III	77	10.69
Class IV	11	1.53
Unclassified	33	4.58
Total	720	100.00

We have been able to classify, according to the functional level, all but 33 of our cases. Table I presents the distribution of all the cases in the various groups. A few of our records bear the terminology of the old classification. In such instances, for the purposes of uniformity of analysis, they have been considered according to the newer adaptation: Class II-A being equal to Class II; Class II-B becoming Class III; and Class III becoming Class IV. In all cases

6. The pelvic architecture played a part in influencing our prognosis. The prognosis becomes progressively worse in the following order; gynecoid, anthropoid, platypelloid, and android.

7. Malposition influenced the prognosis unfavorably.

8. The prognosis in breech presentation is based almost entirely on the pelvic measurements and architecture, and no trial of labor is advised in this presentation. In no case where a vaginal delivery of a breech presentation was advised did such a delivery terminate with fetal mortality.

9. A correct prognosis was given in 97.8 per cent of the series.

10. In only 35 per cent of this series in which dystocia was feared was operative delivery necessary. Sixty-five per cent were given a good prognosis, illustrating the conservative influence of pelvioradiography.

11. The limitations of pelvioradiography are assigned to the difficulty in estimating the soft tissue factors, behavior of the cervix, character of the labor contractions, the skill of the obstetrician, and the age and previous history of the patient.

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TABLE II. PREVIOUS DISEASES

	NUMBER OF CASES	PER CENT OF TOTAL
Rheumatism	311	43.20
Chorea	45	6.24
Rheumatism and chorea	43	5.97
Rheumatism, chorea, and scarlet fever	4	0.56
Scarlet fever	7	0.97
Chorea and scarlet fever	9	1.23
Frequent sore throats	6	0.83
Rheumatic fever, chorea, and scarlet fever	4	0.56
Rheumatic fever and scarlet fever	3	0.42
Diphtheria	3	0.42
Syphilis	2	0.28
Nephritis	2	0.28
Chorea and sore throats	2	0.28
Pott's disease	1	0.14
Nephritis and scarlet fever	1	0.14
Rheumatism and erythema nodosum	1	0.14
Frequent epistaxis	1	0.14
Negative past history	275	38.20
Total	720	100.00

tients had reactivation during their pregnancies. This high incidence emphasizes the importance of obtaining a careful history from each patient.

As would be expected from the preponderance of rheumatic heart disease in our study, mitral lesions accounted for 78.47 per cent of all valvular lesions, and, combined with other lesions, mitral involvement occurred in approximately nine out of every ten cases. In Table III are listed the distribution of the various heart lesions and combinations found in the present analysis.

TABLE III. DISTRIBUTION OF VALVULAR LESIONS

	NUMBER OF CASES	PER CENT OF TOTAL
Mitral stenosis and insufficiency	445	61.81
Mitral stenosis	72	10.00
Mitral insufficiency	48	6.66
Mitral stenosis and insufficiency and aortic insufficiency	48	6.66
Mitral stenosis and insufficiency and aortic stenosis and insufficiency	27	3.75
Aortic stenosis and insufficiency	5	0.69
Aortic insufficiency	3	0.42
Aortic stenosis	1	0.14
Mitral insufficiency and aortic stenosis	1	0.14
Mitral insufficiency and aortic stenosis and insufficiency	2	0.28
Mitral stenosis and aortic insufficiency	3	0.42
Pulmonary stenosis	6	0.83
Congenital lesion	22	3.06
Chronic valvular (hypertensive)	15	2.08
Coronary disease	3	0.42
Paroxysmal tachycardia	6	0.83
Ventricular premature contractions	1	0.14
Unknown	12	1.67
Total	720	100.00

It is a common impression that labor in cardiac patients is of shorter duration than that in noncardiac patients. An analysis of our figures does not entirely bear out this belief. The average length of labor in 260 primiparas with heart disease was found to be 20 $\frac{2}{60}$  hours, and in 332 multiparas 8 $\frac{4}{60}$  hours, as compared with the normal given by Stander<sup>3</sup> as eighteen and twelve hours, respectively. Moreover, no appreciable difference was noted in the length of labor among the various cardiac classes.

we have tabulated the classification recorded at the time of delivery or interruption of the pregnancy. In some instances this was different from that recorded at the initial visit, due to the progress of the disease.

A classification as to etiologic types has been carried out. In Fig. 1, the rheumatic group of 656 cases is shown to represent 91.15 per cent of the total. Of these, 259 were in Class I, 295 in Class II, 76 in Class III, 10 in Class IV, and 16 unclassified. Congenital heart disease in 31 cases accounted for 4.31 per cent, and in this group, except for six unclassified cases, 13 were in Class I, and 12 in Class II. Hypertensive disease was found to be the basis for cardiac trouble in 16 patients or 2.22 per cent; 13 of these were considered as Class II,

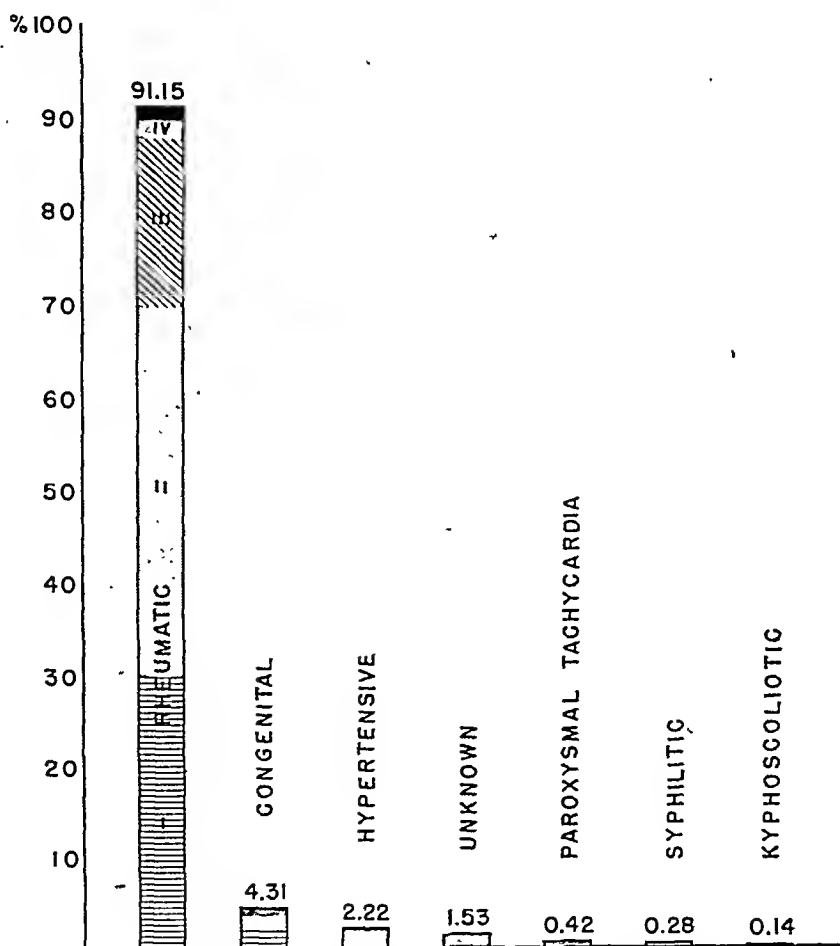


Fig. 1.—Etiologic distribution of heart disease in 720 cases.

one as Class IV, and two unclassified. The type of heart disease was unknown and unclassified in a group of 11 cases, 1.53 per cent. There were three cases, 0.42 per cent, of unexplainable paroxysmal tachycardia; these were not functionally listed, but were presumably Class I. Syphilitic heart disease occurred in two patients, 0.28 per cent; one was in Class I and the other in Class II. Lastly, heart disease was found in association with kyphoscoliosis in three pregnant women, but in only one, Class I, was there found to be an etiologic relation.

Table II presents various diseases that occurred in the past history of our cardiac patients. A history of rheumatic fever in one or more of its manifestations was noted in almost 60 per cent of the entire series, and two of these pa-

TABLE IV. TREATMENT OF CARDIAC DISEASE IN 712 PATIENTS

	TOTAL CASES	INCI- DENCE	INDICATIONS			
			CARDIAC		OTHER	
			CASES	INCI- DENCE	CASES	INCI- DENCE
<i>Abortions.</i> —						
Spontaneous	27	3.78				
Operative	74	10.40	59	8.29	15	2.11
Miniature cesarean section	15	2.11	15	2.11	0	0
Completion incomplete abortion	11	1.55	0	0	11	1.55
Therapeutic curettage	44	6.18	44	6.18	0	0
Salpingectomy (ectopic)	3	0.42	0	0	3	0.42
Hysterectomy	1	0.14	0	0	1	0.14
Total	101	14.18	59	8.29	15	2.11
<i>Deliveries.</i> —						
Spontaneous	404	56.74				
Operative	207	29.08	140	19.68	69	9.69
Low forceps	141	19.81	117	16.44	24	3.37
Midforceps	21	2.95	12	1.69	9	1.27
Cesarean section	21	2.95	11	1.55	10	1.40
Breech extraction	18	2.53	0	0	18	2.53
Manual removal of placenta	6	0.84	0	0	6	0.84
Version and extraction	1	0.14	0	0	1	0.14
Craniotomy	1	0.14	0	0	1	0.14
Total	611	85.82	140	19.68	69	9.69
Grand Total	712	100.00	199	27.97	84	11.80

TABLE V. INCIDENCE OF OPERATIVE DELIVERIES

CLASS	NUMBER OF DELIVERIES	OPERATIVE DELIVERIES	
		NUMBER	INCIDENCE
I	256	62	24.21
II	282	96	34.02
III and IV	44	31	70.43
Total	582	189	32.48

It is well to note that 9.67 per cent of the group had operative deliveries for indications other than cardiac disease. In certain additional instances, while cardiac indications were given, other factors existed which influenced the type of procedure employed.

The percentage of operative deliveries according to functional classification is given in Table V. Even though an approximate 10 per cent be subtracted from each group as having been performed for indications other than cardiac disease, it is apparent that three times as many operative deliveries were performed for cardiac reasons in Classes III and IV as in Class I. The teaching of this clinic, as illustrated by the incidence of operative deliveries in Class I, is that added work of the heart in the second stage of labor can be spared by early and judicious operative means. We further recommend that operative deliveries of cardiac patients be carried out under local anesthesia such as outlined by Griffin and Benson.<sup>6</sup>

<sup>6</sup> The cardiac patient in labor requires continued vigilance, and particular attention must be given to the pulse and respiration rate as pointed out by Mendelson and Pardee.<sup>7</sup> All patients who, in the first stage of labor, have an elevation in pulse rate above 110 or respiratory rate above 24 are digitalized, if this has not already been effected. Administration of oxygen by mask or tent, and other supportive measures, such as Fowler's position, are given when there are symptoms or findings of impending failure.

### Treatment

Our treatment of the woman whose pregnancy is complicated by heart disease is based on the patient's cardiac history, the functional capacity of the heart, and, to a lesser degree, the type of cardiac involvement. We believe that emphasis on the particular valvular lesion is not justified, and agree with Hamilton and Thompson<sup>4</sup> that "prognosis in pregnancy is only slightly affected by differences in the valves involved." However, the history of, or the presence of, cardiac decompensation or auricular fibrillation is of great significance, and may be a legitimate indication for the interruption of the present pregnancy and prevention of future pregnancies.

It is our practice to evaluate each patient when first seen, and in the more advanced cases this requires hospital study. Those patients who may safely be allowed to continue their pregnancies are followed at frequent intervals in a special Cardiac Clinic maintained in the Lying-In Hospital. Certain other patients with more serious heart disease may be kept in the hospital throughout the remainder of their pregnancies.

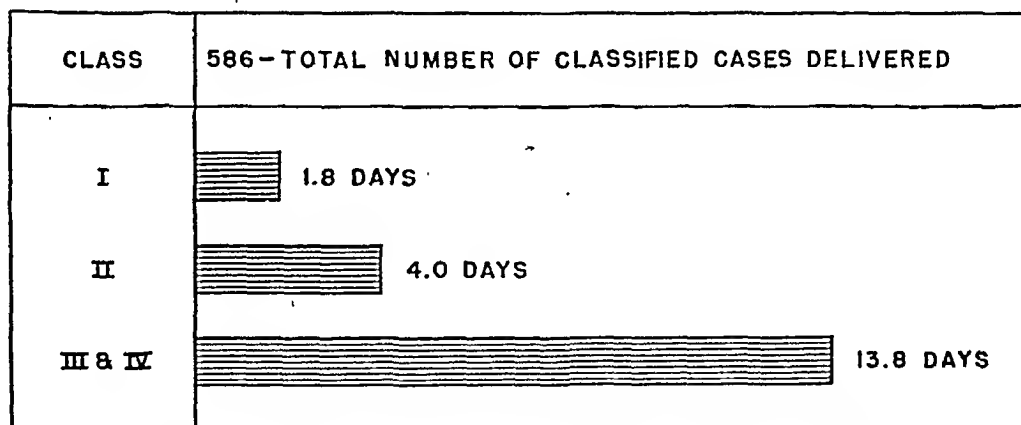


Fig. 2.—Average duration of hospitalization prior to delivery.

We are convinced that hospitalization prior to delivery is an important factor in obtaining a low mortality rate in cardiac patients. Consequently, it is our rule to admit prior to labor all patients in Classes III and IV, and selected patients in Classes I and II. The average duration of predelivery hospitalization is shown in Fig. 2. Classes III and IV have been combined because of the small number of cases in Class IV.

A summary of our treatment of patients with heart disease is presented in Table IV. Of the 712 patients, 14.18 per cent terminated as abortions, of which 8.29 per cent were operative and performed because of cardiac indications. This latter figure is in sharp contrast to the 2.87 per cent incidence of therapeutic abortion in the previous five-year period. Among the full-term and premature deliveries 29.08 per cent were operative, a figure practically identical to that of the former study. The incidence of forceps deliveries, 18.13 per cent, shows an increase in the use of this procedure when compared with 11.96 per cent in the former study. This is partially compensated by a reduction in the incidence of cesarean sections, from 4.07 per cent to 1.55 per cent. The wisdom of such a trend has been well proved in a recent paper by Mendelson.<sup>5</sup>



Of further interest and importance in the maternal mortality is the significance of the unregistered patient. Five deaths occurred in the unregistered group of 65 patients, seven times that in the registered group of seven in 655 patients. In Fig. 3 we have graphically shown these findings.

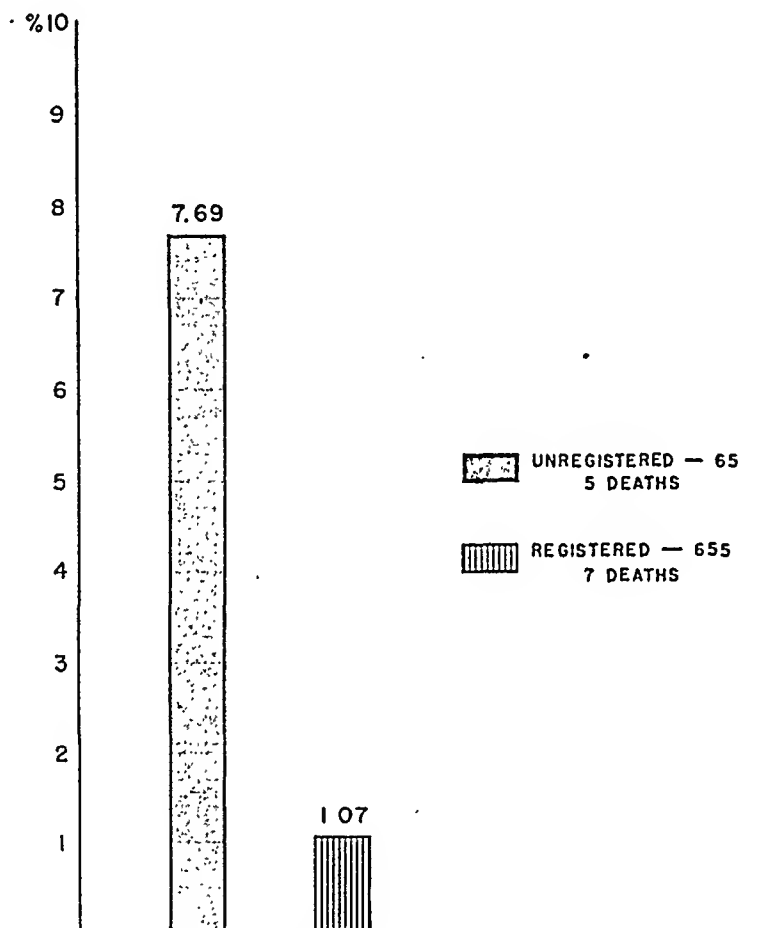


Fig. 3.—Maternal mortality in registered and unregistered patients.

From a review of the nine cardiac deaths listed in Table VIII, it is apparent that death may occur at any time during the pregnancy. The cause of death in six cases was congestive heart failure. One-half of these had preceding upper respiratory infections, a finding reflecting the serious danger of such complications in cardiac patients as previously shown by Oppel.<sup>8</sup> Bacterial endocarditis was the cause of death in two, and coronary occlusion in one other case. Because of the potential hazard of bacterial endocarditis, the prophylactic use of sulfadiazine and penicillin has been advised. Wheeler<sup>9</sup> in a report, not yet published, of 200 cases of subacute bacterial endocarditis found labor as a predisposing factor to death in nine patients, second in importance only to upper respiratory infections.

The infantile mortality among those infants weighing 1,500 grams or over at birth, and including all infants dying during the first fourteen days following birth, was 3.24 per cent. The total clinic figure for the same period was 3.07 per cent. While there is some difference between these two figures, in no instance of the 20 infant deaths reviewed did the maternal cardiac disease seem

## Mortality

Maternal mortality due to heart disease is important, as shown by its present-day position among the major causes of maternal deaths. On the basis of this seven-year study, heart disease was found to be the leading cause of maternal deaths at the Lying-In Hospital (24.33 per cent). Such a prime position does not result from an increasing frequency of heart disease, or from a rise in mortality among our cardiac patients. Its change from a former third position may be said to be due to greater success in our efforts to control and combat infections and hemorrhage. In the treatment of infections marked improvements have resulted since the advent of sulfonamide chemotherapy and penicillin.

TABLE VI. HEART DISEASE IN 37,913 PREGNANCIES

	1932-1937			1937-1944			TOTAL		
	TOTAL CLINIC	CASES	INCIDENCE	TOTAL CLINIC	CASES	INCIDENCE	TOTAL CLINIC	CASES	INCIDENCE
Deliveries	13,140	386	2.86	22,022	611	2.78	35,162	977	2.84
Abortions	915	32	3.49	1,836	101	5.50	2,751	133	4.84
Maternal deaths	45	7	15.55	37	9	24.33	82	16	19.51
Undelivered	9	5	55.55	6	5	83.33	15	10	66.66
Delivered	36	2	5.55	31	4	12.90	67	6	8.95

Table VI compares the patients who have heart disease with the total clinic population for both the five- and seven-year periods, and the total twelve-year period. In each of the periods the ratio of the cardiac to the total clinic deliveries was about the same, and for the twelve-year period averaged 2.84 per cent. The incidence of abortions in cardiac patients was found to be 3.49 per cent in the first five years, and 5.50 per cent in the present seven years, with a twelve-year average of 4.84 per cent. This marked rise is explained by an increased number of therapeutic abortions. In the twelve-year total period 19.51 per cent of the total deaths were due to heart disease, 66.66 per cent of these were undelivered, and 8.95 per cent delivered.

TABLE VII. MATERNAL MORTALITY

	DEATHS	DELIVERIES	PREGNANCIES	DEATHS	
				NUMBER PER 1000 DELIVERIES	NUMBER PER 1000 PREGNANCIES
1932-1937					
Total Clinic	45	13,140	14,055	3.43	3.20
Cardiac	7	386	493	18.22	14.18
1937-1944					
Total Clinic	37	22,022	23,858	1.68	1.55
Cardiac	9	611	712	14.73	12.64
Total 1932-1944					
Total Clinic	82	35,162	37,913	2.33	2.16
Cardiac	16	997	1,205	16.05	13.28

Evidence of improvement in management and treatment of pregnant women can be obtained from comparative studies in mortality rates, as shown in Table VII. This table reveals a halving in the mortality rate of the total clinic population in the present period as compared with the previous period. Among the patients with heart disease there has also been a significant reduction from 14.18 to 12.64 deaths per thousand pregnant cardiac patients.

result from the use of chemotherapy of cardiac patients with respiratory infection and in cardiac patients in labor. The infantile mortality appears unaffected by the maternal heart disease.

### Conclusions

1. Heart disease occurred in 3 per cent of our obstetric patients. Seven hundred and twenty cases were analyzed in the present seven-year study and compared with 418 in the previous five years.

2. According to the New York Heart Association functional classification, 38.48 per cent occurred in Class I, 44.72 per cent in Class II, 10.69 per cent in Class III, and 1.53 per cent in Class IV.

3. Rheumatic heart disease accounted for 91.11 per cent of the total cases of heart disease.

4. History of previous disease was given in 61.80 per cent of the total cases of heart disease. Rheumatic fever in one or more of its manifestations occurred in all but 2.43 per cent.

5. Mitral valvular disease is by far the most common type, but we are not convinced that it is more dangerous than other valvular lesions.

6. Good treatment rests on proper study and evaluation of each patient. Hospitalization prior to labor is of benefit, particularly in severe cardiacs. The greatest dangers are auricular fibrillation and history of decompensation.

7. Therapeutic abortions were performed in greater number in the present seven years, 8.29 per cent, than in the previous five years, 2.87 per cent.

8. Operative deliveries occurred in 29.08 per cent. A greater number of forceps deliveries are now performed, and a smaller number of cesarean sections.

9. Heart disease is the leading cause of maternal deaths in the present seven-year period.

10. Compared with the previous five years the maternal mortality in cardiac patients has been reduced from 14.18 to 12.64 per thousand cardiac patients.

11. The mortality in the unregistered group is seven times that in the registered group.

12. The infantile mortality is essentially unaffected by the maternal heart disease.

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TABLE VIII. CARDIAC MATERNAL DEATHS

NO.	AGE	PAR- ITY	LESION	CLASS	REGIS- TERED	CAUSE OF DEATH
1	26	0	Mitral insufficiency	I	-	Bacterial endocarditis and thrombo- sis of superior sagittal sinus at 9 weeks. Patient undelivered
2	36	1	Mitral stenosis and in- sufficiency	II(?)	+	Congestive failure following mini- ature cesarean section at 15 weeks
3	23	0	Mitral stenosis and in- sufficiency	II	+	Subacute bacterial endocarditis ( <i>Streptococcus viridans</i> ). Death 16 days postpartum
4	32	2	Mitral stenosis and in- sufficiency; auricular fibrillation	IV	-	Congestive failure preceded by bron- chopneumonia. Death followed miniature cesarean section at 22 weeks
5	36	1	Mitral stenosis and in- sufficiency	IV	+	Congestive failure preceded by upper respiratory infection. Death fol- lowed at 24 weeks, patient unde- livered
6	31	1	Mitral stenosis and in- sufficiency; aortic ste- nosis and insufficiency	IV	-	Congestive failure at 32 weeks. Pa- tient undelivered
7	34	2	Mitral stenosis and in- sufficiency; auricular fibrillation	IV	-	Congestive failure following dilata- tion and curettage at 13 weeks
8	21	0	Mitral stenosis and in- sufficiency	IV $\frac{1}{2}$	+	Congestive failure following broncho- pneumonia. Death at 30 weeks, patient undelivered
9	35	3	Coronary sclerosis	Unclassi- fied	+	Coronary occlusion. Death at 39 weeks. Patient undelivered

to play a role. In the previous study by Stander, it was his conclusion that maternal heart disease does not increase the infantile mortality. The same impression is gained from this study.

### Summary

Heart disease is a most serious complication of pregnancy. In the 37,913 obstetric patients seen in this clinic in the past twelve years there have been 1,138 with heart disease, an incidence of 3 per cent. As in the past, we have found the functional classification of the New York Heart Association adaptable to the care and evaluation of our patients. Data has been tabulated regarding functional classification, etiologic types of heart disease, previous diseases, and distribution of valvular lesions.

In treating cardiac patients we again emphasize the importance of hospitalization prior to labor. Special care must be given to these women in labor, and the figures bear out our recommendation that the second stage be shortened by operative means, particularly in the severe cardiac. We have noted a trend from cesarean to forceps deliveries, a greater use of local anesthesia, and an evident liberalization in interruption of pregnancies in bad risk cardiacs. These factors explain a lowering of the maternal mortality among cardiac patients from 14.18 to 12.64 per thousand pregnancies. A further lowering of this figure is possible through better cooperation in early registration, and also presumably through improvement in selection of patients for therapeutic abortion, earlier interruption, and judicious sterilization. Perhaps also an improvement will

TABLE I. RESULTS OF TREATMENT OF ECLAMPSIA WITH VERATRUM VIRIDE

AUTHOR	NUMBER OF CASES	VERATRUM VIRIDE ONLY	VERATRUM VIRIDE PLUS OTHER DRUGS AND/OR INDUCTION	RECOVERED	DIED	PER CENT MORTALITY
Baker, 1859 <sup>1</sup>	1		1	1	0	0
Fearn, 1871 <sup>24</sup>	13	3		3	0	0
			10	9	1	10
Jewett, 1887 <sup>10</sup>	22	22		16	6	27
Trimble, 1890 <sup>25</sup>	26	15		14	1	6.7
			11	9	2	18
Ryder, 1906 <sup>6</sup>	13			10	3	23
Gillespie, 1911 <sup>27</sup>	18	18		14	4	22
Zinke, 1913 <sup>26</sup>	30		30			13.3
Haultaine, 1916 <sup>28</sup>	38			36	2	5.3
Stevens, 1922 <sup>21</sup>	25		25	21	4	16
Bryant, 1935 <sup>3</sup>	121		121	109	12	9.9
Bryant-Fleming, 1940 <sup>4</sup>	120		120	118	2	1.7

Among those opposed to the use of the drug was Potter,<sup>7</sup> who stated that it was "... dangerous, deceptive, and uncertain in its action. It is but a symptomatic remedy at best. ... It reduces arterial tension and cardiac pressure without exercising special influence over the progress of the malady. ... I am afraid that many cases of eclampsia have succumbed to the indiscreet employment of *Veratrum*. ...". Kemper,<sup>8</sup> in discussing a paper in 1899, stated that *veratrum viride* was unsatisfactory, and that any case which could be controlled by any medication would yield to chloral and chloroform.

Impressed by the results of the treatment of eclampsia reported by Bryant and Fleming, the author initiated a series of physiologic and clinical studies in an attempt to localize more accurately the site of action of the drug, and to evaluate its use in the treatment of the hypertensive toxemias of pregnancy. The results of the initial phases of the investigation have been reported previously.<sup>9-11</sup> In this paper the results of the treatment of a group of patients with hypertensive toxemias of pregnancy by *veratrum viride* alone will be reported.

### Material

A total of 12 patients was studied. The duration of pregnancy in nine patients not in labor varied between thirty-two and thirty-seven weeks; eight were primigravidas, and all except one had pre-eclampsia. The remaining three were in labor and, of these, one had chronic hypertensive disease with an associated pregnancy. The latter had had an abruptio placenta with a previous pregnancy and, during the prenatal period of this pregnancy, slight elevations in blood pressure had been noted on several occasions.

### Method

*Prenatal Patients.*—All had been confined to bed for at least twenty-four hours prior to the administration of the drug. No medication was given, but all were receiving a salt-poor diet (less than 2 Gm. of NaCl daily). Control periods during which blood pressure, pulse rate, and half-hourly urine output were observed varied from four to twenty-four hours. In each instance the fluid intake was sufficient to maintain an adequate output of urine by a normally functioning kidney. The drug, veratrone (an aqueous solution of *veratrum viride* prepared by Parke, Davis & Co.), was injected intramuscularly at the end

## VERATRUM VIRIDE IN THE TREATMENT OF THE TOXEMIAS OF PREGNANCY

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**A**LTERATIONS in the routine for the treatment of any disease follow increased knowledge concerning the malady. In obstetrics, as in all the other specialties, however, old methods of therapy discarded by our predecessors are periodically "discovered" and advanced as the answer to some particular poorly understood problem. Such is the history of *veratrum viride* in the treatment of eclampsia.

Baker<sup>1</sup> who appears to have been one of the first to apply the drug in the treatment of eclampsia (1859) was prompted to publish his experiences with its use by an article which stated that "*veratrum viride* has seen its day." In a discussion of various remedies which might be utilized to control eclampsia, Winter<sup>2</sup> stated concerning *veratrum viride* "... in the onward march of medical science it seems to have been lost sight of until comparatively recently, when writers seem to vie with each other in extolling its virtues. ..." For several years after this the drug was extensively used but again it gradually was discarded in favor of newer methods. Bryant,<sup>3</sup> in 1935, and Bryant and Fleming,<sup>4</sup> in 1940, again urged its use as an adjunct to the treatment of eclampsia, principally because of its vasodilating properties, thus initiating new surge of interest in its application to this condition.

The results obtained from the administration of *veratrum viride* to toxemia patients over a period of eighty-five years are, at least on the surface, good. It must be remembered, however, that for much of this time diagnosis was inexact and many of the cases of "eclamptic convulsions" were from other causes, i.e., epilepsy, nephritis, hypertensive encephalopathy, etc. Likewise, as Zinke<sup>5</sup> so aptly pointed out, the course of eclampsia may vary in different individuals. He described three types: (1) *malignant*, which is fatal from the beginning despite adequate treatment; (2) *benign*, from which the patient will recover regardless of what is done for (or to) her; and (3) those cases of *mean gravity*, which are influenced by judicious treatment. Ryder<sup>6</sup> also was aware of variations in the course of the disease, dependent upon circumstances other than the treatment. He noted in his series of 37 cases, all treated by much the same method, that the death rate varied with the seasons of the year: of 14 women treated in the fall, two died; of eight treated in the late spring, one died; while of 15 treated during the winter, eight failed to survive.

From a review of the numerous papers written on the treatment of eclampsia with *veratrum viride* since the middle of the last century, it becomes obvious that opinion concerning its efficacy is divided. While certain men were enthusiastic, many more considered the drug to be of little or no value. The final results are clouded by the fact that in most instances other drugs (morphine, chloral hydrate, bromides, chloroform) were usually used in conjunction with veratrum, and because the writers did not attempt to classify the cases either as to severity or relationship to delivery (Table I).

TABLE II

CASE	NUMBER	AGE YEARS	PARA GRAVIDA	DURATION PREG- NANCY WEEKS	AVERAGE CONTROL BLOOD PRESSURE MM. HG.	AVERAGE URINE VOLUME (C.G. PER 1/2 HOUR) CONTROL	AVERAGE URINE VOLUME (C.G. PER 1/2 HOUR) INJECTION	AVERAGE BLOOD PRESSURE AFTER INJECTION	LOWEST BLOOD PRESSURE	AVERAGE PULSE RATE AFTER INJECTION	UREA CLEAR- ANCE (C.G. PER MIN.) CONTROL	UREA CLEARANCE (C.G. PER MIN.) AFTER INJECTION
<i>Prenatal</i>												
(1)	315856	29	0	34	165/110	69.0	67.0	120/90	110/85	64	41	32.0
(2)	334292	29	0	34	165/110	30.0	16.2	130/85	110/75	58		
(3)	332897	26	0	36	150/110	31.6	23.6	115/85	100/80	70		
(4)	329832	19	0	36	150/110	88.6	59.0	120/80	100/70	50		
(5)	318412	18	0	36	170/120	63.6	19.5	130/85	100/60		26	9.8
(6)	302266	25	0	37	168/120	25.0	6.5	130/86	100/70	60	45	29.0
(7)	324495	23	0	32	190/120	7.5	3.4	140/95	120/70	58		
(8)	353540	23	0	37	180/130	103.0	72.0	110/70	80/40	60	83	27.0
(9)	329896	39	v vi	8	180/120	55.1	51.4	140/95	90/60	73		
<i>Patients in Labor</i>												
(10)	355548		0	40	150/100	18.2	18.8	135/90	100/80	58		
(11)	340876		0	36	170/115	21.0	20.0	180/120	175/120	75		
(12)	355241		i ii	40	150/100	33.3	2.6	130/85	110/70	79		

of the control period, usually in a dosage of 0.5 c.c. Subsequent injections were of 0.25 to 0.5 c.c., and were given as indicated by a rise in blood pressure.

*Patients in Labor.*—The three patients in labor had been observed for three to ten hours prior to the injection of the drug. During this time frequent recordings of blood pressure and pulse rate were made, and the urine output and fluid intake were measured. The initial injection of veratrone was 0.5 c.c., and subsequent injections varied from 0.25 to 0.5 c.c. The records of fluid intake and output, blood pressure, and pulse rate were continued.

The observations in both groups were continued for periods varying from six to twenty-two hours, at which time the experiment was terminated. Only three patients were studied for less than ten hours, two of these for nine hours, and one for 6 hours; in each instance the drug was discontinued because of a markedly decreased urinary output. All urine specimens were collected by catheter, the bladder being completely emptied each time.

### Results

*Blood Pressure.*—In the prenatal patients the blood pressures were substantially reduced in each instance (Table II). The pressure was kept below the preinjection level for periods varying from six to twenty-two hours, at the end of which time the observations were terminated. As has been reported previously<sup>11</sup> the drop in blood pressure was easy to obtain in those patients with pre-eclampsia. An initial effect often was noted within ten to fifteen minutes of the injection, with the lowest level following in about one hundred and twenty minutes. Shortly after the most marked depression, the systolic blood pressure usually rose 10 to 30 mm. Hg, where it became temporarily stabilized. As the effect of the drug diminished, the blood pressure gradually increased, but repeat injection usually resulted in a secondary fall.

The reduction of blood pressure was somewhat less striking in those patients who were in labor (Table II). In one (Case 11), the pressure increased despite the fact that the pulse rate was depressed.

*Pulse Rate.*—The highest average pulse rate following administration of the drug in the prenatal patients was 73 beats per minute. The lowest pulse rate recorded was 44 beats per minute. As reported previously, the pulse in most instances returned to the preinjection rate before a marked rise in blood pressure was noted.

The pulse rate remained higher in the patients in labor than in the prenatal cases. The reduction in this group was most marked in a patient with pre-eclampsia (Case 10).

*Urine Volume.*—In all the patients not in labor, the injection of the drug was followed by a reduction in urine volume. In two instances this reduction was slight (Cases 1 and 9); in four patients, however, urine output reached a dangerously low level. One (Case 8) produced 55 c.c. in eight hours (three hours anuria); Case 5 produced 62 c.c. in four hours (three hours anuria); Case 6 produced 81 c.c. in six hours (two hours anuria); and Case 7 produced 75 c.c. in nine hours (six hours anuria) (Fig. 1). A comparison of control 24-hour urine volumes with those while the drug was being given is shown in Fig. 2. During the entire period in which the blood pressure was kept below its usual level by the drug, the urine output was diminished as compared to that of the control day. As the blood pressure rose however, there occurred an increase in urine volume to compensate for the delayed excretion. The total for the 24-hour test period was substantially the same as that during the control day, since the diuresis was not sustained. Essentially the same results were noted in other patients studied in an identical manner. However, in two instances the total daily output was definitely diminished as a result of administration of Veratrone (Table III).





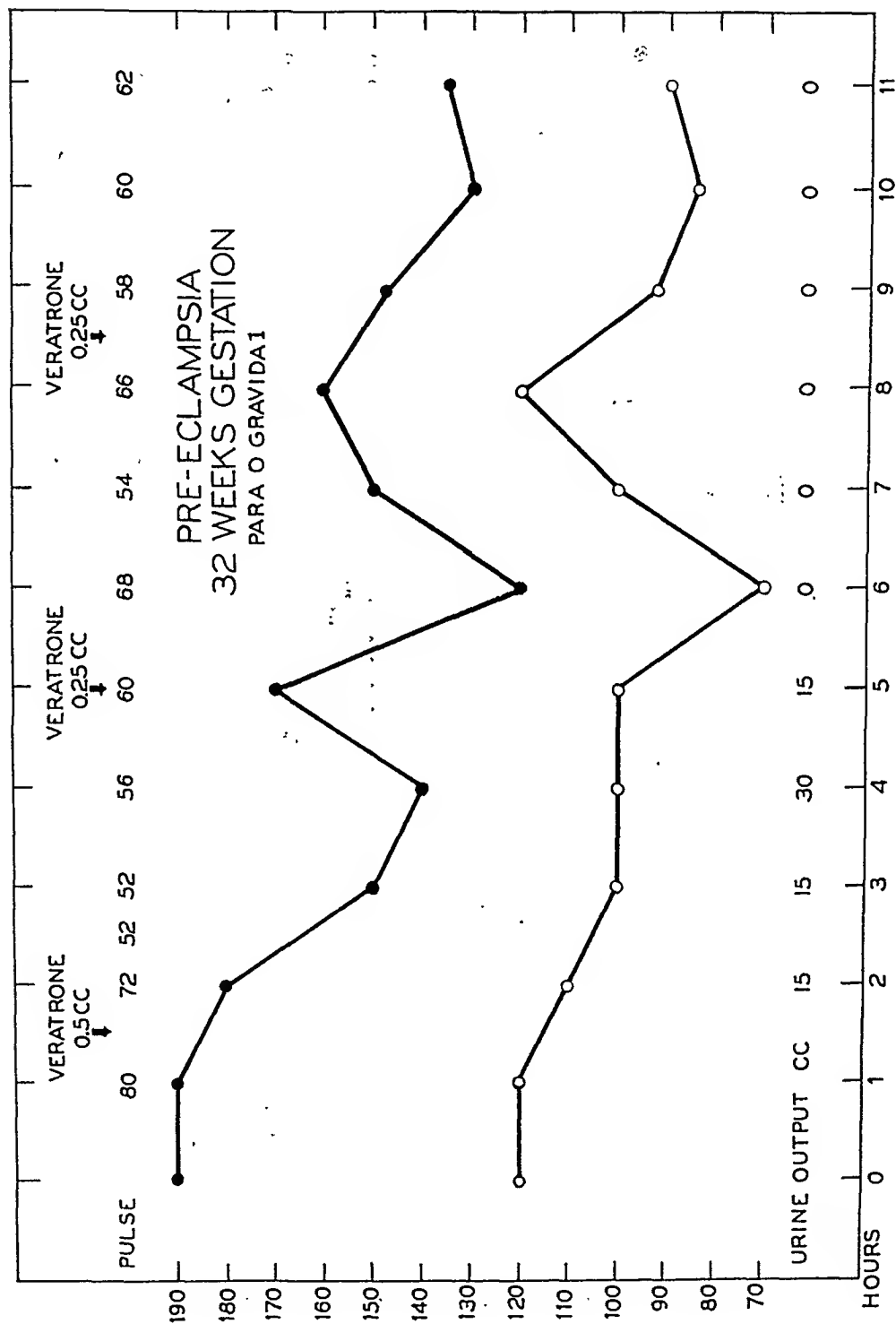


Fig. 1.



TABLE III. 24-HOUR URINE VOLUMES IN PRE-ECLAMPSIA AS INFLUENCED BY THE ADMINISTRATION OF VERATRUM VIRIDE

TIME	CONTROL DAY		TEST DAY	
	INTAKE (C.C.)	OUTPUT (C.C.)	INTAKE (C.C.)	OUTPUT (C.C.)
I. 6 A.M. to 12 N.	600	320	500	210
12 N. to 6 P.M.	700	780	500	240
6 P.M. to 12 M.	500	350	500	210
12 M. to 6 A.M.	120	60	120	120
	1920	1510	1620	780
II. 6 A.M. to 12 N.	2400	1810	2200	797
12 N. to 6 P.M.	700	1140	800	403
6 P.M. to 12 M.	200	731	400	1100
12 M. to 6 A.M.	0	495	200	525
	3300	4176	3600	2825
III. 7 A.M. to 12 N.	2250	2190	2250	1103
12 N. to 8 P.M.	550	270	550	740
8 P.M. to 12 M.	400	140	400	355
12 M. to 7 A.M.	0	205	0	275
	3200	2805	3200	2473
IV. 10 A.M. to 4 P.M.	600	350	600	290
4 P.M. to 10 P.M.	900	460	900	260
10 P.M. to 4 A.M.	0	310	0	290
4 A.M. to 10 A.M.	300	395	300	295
	1800	1515	1800	1135

The urine volume in patients Nos. 10 and 11 was not significantly altered by the drug, however, there occurred a marked reduction in patient No. 12. In the latter only 37 c.c. of urine were excreted during the six hours of Veratrone administration.

No ill effects were noted as far as the babies were concerned. There was no interference with the mechanism of labor in any of the patients who were in labor. No instances of circulatory collapse were encountered, but vomiting occurred commonly.

### Discussion

Any program of treatment for the patient with pre-eclampsia or eclampsia must include measures directed toward control of convulsions and maintenance, or stimulation of renal function; reduction of blood pressure is of less importance and is usually necessary only if it reaches a dangerously high level. The pregnancy must, at least in the initial stages of treatment, assume a position of secondary importance unless the patient is in active labor. Since no single drug is known which will satisfactorily accomplish all these things, a combination of medications is utilized in most standard treatment regimes. The barbiturates, magnesium sulfate and morphine, when administered in adequate dosages, will control the convulsions and the hypertension in most cases. Of more importance than this, however, is the maintenance of adequate urine production either in the severe pre-eclamptic to aid in preventing eclampsia, or as a definitive step in treatment in the latter condition. Reduction of blood pressure even to normal levels in these conditions may result in definite

be detrimental. Older authors state unequivocally that its use likewise controls convulsion. Brodhead<sup>15</sup> maintained that "There can be no question that the drug will usually control convulsions if the pulse can be lowered to about 60," and Jewett<sup>16</sup> that "Convulsions cannot occur with a pulse less than 60." Since the more modern writers have for the most part used *veratrum viride* only as an additional drug in the treatment of eclampsia, recent results referable to control of convulsions are unreliable.

The reduction of urine volume in the pre-eclamptic patients treated with *veratrum viride* alone is striking. In a previous paper<sup>11</sup> the author reported a maximum reduction of 95.7 per cent in a group of such patients after the administration of the drug. This was likewise observed in this series. *At no time was the injection of veratrum viride followed by an increase in urine output*, and in four instances it was felt that the patient was dangerously close to eclampsia as a result of failure to excrete urine. All responded, however, to the prompt administration of glucose.

Bourne,<sup>17</sup> in 1922, reporting a case of eclampsia treated with veratrone, stated that the urine output was increased after the drug was administered. The urine volumes during the 2-day treatment period, however, varied from 40 to 150 c.c. every four hours, with the exception of the last four hours before delivery when 360 c.c. were excreted. Each drop in blood pressure produced by an injection of veratrone was followed by a diminution in urine volume which increased as the blood pressure rose (Fig. 4).

This renal failure may be explained by several factors, the first of which is the blood pressure. If the level of the systemic pressure is reduced to a point at which the renal blood pressure is below that necessary for glomerular filtration, urine excretion will cease. It appears from these studies that the lowest pressure necessary to carry on kidney function is higher in pre-eclampsia than in normal pregnancy. The second factor is blood volume: in severe pre-eclampsia and eclampsia the blood is concentrated due to withdrawal of water to the tissues, and any increase in renal output must of necessity be preceded by blood dilution. That this does not occur following the administration of *veratrum viride* is demonstrated by the fact that in a small group of patients in whom the hematocrit and serum proteins were determined both before and during veratrone therapy, no alteration was noted.<sup>18</sup> The third action of the drug which may depress renal function is its effect on the circulation time. This was increased in some instances to double that during the control period;<sup>18</sup> thus less blood is being delivered to the glomeruli for filtration.

The addition of *veratrum viride* to standard treatment routines has resulted in no marked increase in maternal salvage. MacCallum,<sup>19</sup> in 1887, in discussing Oatman's paper, reported 14 consecutive cases to whom no veratrum was given without mortality. Solomons,<sup>20</sup> in 1922, had a 10 per cent mortality in 204 cases treated by starvation, stomach lavage, magnesium sulfate, sodium bicarbonate enemas, and morphine, as compared to a report by Stevens<sup>21</sup> in the same year of 25 patients treated by *veratrum viride* and induction of labor with a 16 per cent death rate. In 1935, Bryant<sup>3</sup> reported a mortality rate of 10 per cent for 121

while the pressure remains at a level as high as that prior to delivery, at which time urine excretion may have been markedly impaired. Thus, it seems probable that the hypertension is beneficial in maintaining kidney function, and that only in the severe pre-eclamptic or eclamptic is it unable to compensate for the abnormal renal physiology. The intravenous injection of hypertonic glucose

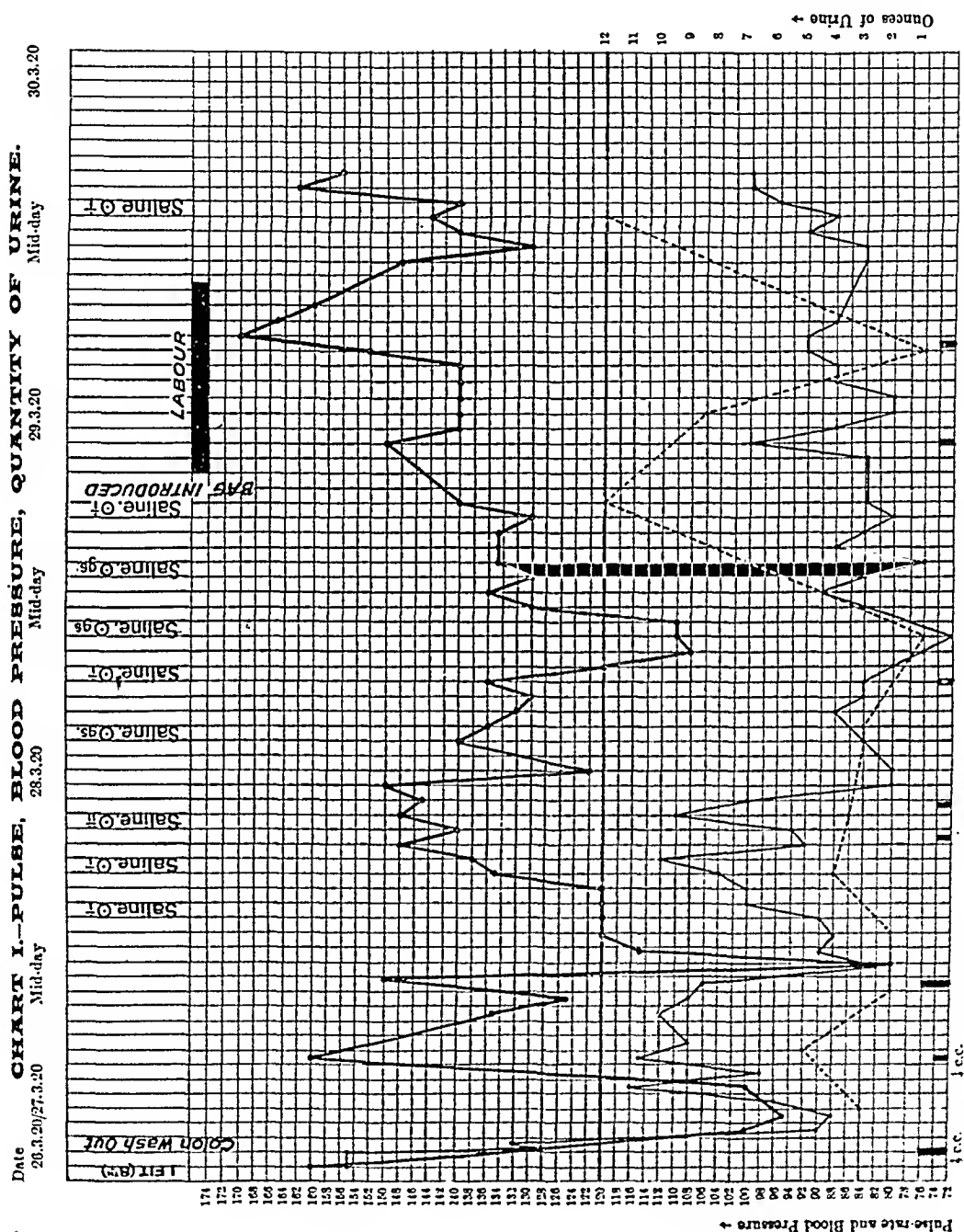


Fig. 4.—(Reprinted with permission—J. Obst. & Gynaec. Brit. Emp. 29: 432, 1922.)

solutions is by far the most effective method of insuring adequate renal function; Dieckmann<sup>14</sup> states that the introduction of the use of such solutions was one of the outstanding contributions to the treatment of eclampsia.

*Veratrum viride* meets the requirements for the treatment of toxemia only in that it will reduce the blood pressure which, as pointed out above, may

## THE TREATMENT WITH MASSIVE ARSENOTHERAPY OF EARLY SYPHILIS COMPLICATED BY PREGNANCY

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THE transmission of syphilis from mother to fetus should be preventable. However, in spite of this, prenatal syphilis still remains a fetocidal and stigmatizing disease because syphilis in the mother is unrecognized, untreated, or poorly treated. Inadequate treatment may be due to the choice of drugs or the plan used in their administration. It often is a result of insufficient time, after diagnosis is made, to give adequate protective therapy. Laxity on the part of the patient in receiving the outlined therapy may also be a factor. Rapid treatment should solve all of these problems.

In a large series of pregnant, untreated, latent syphilitic women, Jeans<sup>1</sup> found only 16.9 per cent of their infants were nonsyphilitic. Thirty and three-tenths per cent of their conceptions either terminated in abortions or stillbirths. Infant mortality was 30.2 per cent. Twenty-four per cent of the children of these mothers were stigmatized with congenital syphilis. Comparing these figures with the average incidence of fetal mortality in normal women, Jeans reported 76 per cent delivered healthy infants, 15 per cent of the infants died in infancy, and 9.7 per cent of the pregnancies resulted in miscarriages or stillbirths.

Marshall's<sup>2</sup> report on early syphilis (infections of less than five years' duration) without antisymphilitic treatment complicated by pregnancy is somewhat similar. Twenty-two per cent of the children were normal; 48 per cent of the pregnancies resulted in miscarriages or stillbirths, and 30 per cent were syphilitic infants. In another series of pregnant women with syphilis treated with 2.3 Gm. of arsphenamine and 0.5 Gm. of mercuric salicylate during the pregnancy, 65 per cent of the infants were normal; 6 per cent of the pregnancies resulted in abortions, and 8 per cent in stillbirths. Twenty-one per cent of the infants had syphilis.

McKelvey and Turner<sup>3</sup> reported their study of a series of pregnant women with latent syphilis, who received a total of 2.0 Gm. of arsphenamine during the second and third trimester of pregnancy. Seventy-eight per cent of the infants born of these mothers were normal and 22 per cent had syphilis. When 2.0 Gm. of arsphenamine plus mercury or bismuth were given during the second and third trimesters, the rate of normal infants increased to 93.4 per cent, and the syphilitic infant percentile decreased to 6.6. When a total of 4.0 Gm. of arsphenamine was given during any stage of the pregnancy, approximately 100 per cent of the infants were normal. If treatment was not started until the last trimester with weekly injections of arsenic and bismuth, 77.7 per cent of the infants were normal and 22.2 per cent had syphilis. If no treatment was given to the mothers, 64.5 per cent of the infants born of these mothers had syphilis.

Castallo, Coppolino, Rakoff, Roeder, and Dickson<sup>4</sup> found that if 240 mg. of mapharsen and 360 mg. of bismuth were given to late latent pregnant women, 90.7 per cent of their children were live births, 7 per cent stillbirths, and 2.3

patients, and in 1940 with Fleming,<sup>4</sup> a mortality of 1.7 per cent in 120 cases in which veratrum was used in addition to sedation, glucose, and induction of labor, while in 1945 Arnell<sup>22</sup> reported 142 consecutive cases of eclampsia without a fatality, no *veratrum viride* being administered. The combined mortality rate for 86 patients treated at the Chicago Lying-in Hospital, and 52 patients treated at the St. Louis Maternity Hospital under the supervision of Dieckmann is 10 per cent.<sup>23</sup> *Veratrum viride* was not used.

The results reported in this and previous publications indicate that on a purely physiologic basis *veratrum viride* produces an effect exactly opposite that which is desired for a rational therapeutic regime for eclampsia. Although eclamptic patients have not been studied under the conditions reported here, it seems unlikely that the drug would have a beneficial effect on a disease which, with the exception of the convulsions, is identical to severe pre-eclampsia in which *veratrum viride* does nothing to improve the abnormal vascular-renal physiology.

### Conclusions

1. *Veratrum viride* was administered to a group of patients with pre-eclampsia and hypertension complicating pregnancy both before and during labor. No other drug was used.

2. The blood pressure and pulse rates in the pre-eclamptic patients were consistently reduced, but apparently to the detriment of adequate renal function, an undesirable consequence in these individuals.

3. The good results in series of patients treated with *veratrum viride* can be duplicated in series in which the drug was not used.      3

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lieved, would be as effective but less dangerous. Two hundred and forty milligrams of mapharsen were dissolved in 2,000 c.c. of 5 per cent glucose and administered by slow drip intravenously the first day, and then 120 mg. of mapharsen in 1,000 c.c. of 5 per cent glucose intravenously for the next seven days, making a total of 1,080 mg. of mapharsen. This solution was delivered at the rate of 2 c.c. per minute. In addition to the mapharsen, 130 mg. of bismuth subsalicylate in oil were injected intramuscularly on the first, third, sixth, and ninth days. Using this regimen, we treated ten cases of early syphilis complicated by pregnancy.\*

Before treatment was started, the following procedures were routinely done: a complete routine physical examination, including a dark-field examination of syphilitic lesions, if present; a Kahn quantitative blood serologic test for syphilis, and a spinal fluid examination, regardless of the stage of pregnancy. A chest roentgenogram, a bromsulfalein test, and a phenolsulfonphthalein test were done to make sure no liver or kidney damage was present. No patient with abnormalities in the latter two procedures was given massive arsenotherapy. A routine blood count and urine examination were performed on each patient.

TABLE I. RESULTS OF MASSIVE CHEMOTHERAPY ON FORTY PREGNANT WOMEN WITH SYPHILIS ON THIRTY-EIGHT OF THEIR INFANTS

SYPHILIS	AGE OF PREG- NANCY	PREG- NANT WOMEN	MOTHERS' SEROLOGIC TITER	CORD BLOOD SEROLOGIC TEST			BLOOD SERONEGATIVITY MAINTAINED BY		INFANTS NOT FOL- LOWED
TYPE	TRIMES- TER	NUM- BER	UNITS	NEG.	N.D.	UNITS	MOTHERS	INFANTS	NUMBER
				NO.	NO.	NO.	MONTHS	MONTHS	
Primary	First	2	0 to 80	1	1	-	16 to 18	3 to 18	
	Second	1	0	1	1	-	10	12	
	Third	1	40	1	1	-	15	18	
Early secondary	First	6	40 to 320	5	1	-	8 to 27	3 to 8 <sup>§</sup>	1
	Second	14	40 to 160	7	7	-	8 to 27	3 to 27 <sup>  </sup>	1
	Third	7	40 to 280	7	-	-	8 to 27	3 to 24 <sup>¶</sup>	1
Late secondary	First	0	-	-	-	-	-	-	
	Second	1	560	1	-	-(1)	12	8	
	Third	1	80	-	-	4	27	24	
Early latent	First	1	40	1	-	-(1)	18*	4	
	Second	4	40 to 120	4	-	3(1)	24 and 33 <sup>†</sup>	8 to 21	
	Third	1	80	-	-	4	36 <sup>‡</sup>	6	
Congenital	First	0	-	-	-	-	-	-	
	Second	1	80	1	-	-	14	3	
	Third	0	-	-	-	-	-	-	

\*1 Mother had 4 units at eighteen months.

†2 Mothers had 4 units at twenty-four and thirty-three months.

‡1 Mother had 4 units at thirty-six months.

§1 Child died at the age of seven days. Autopsy virus enteritis. No syphilis.

||1 Child died at the age of three months. Serology negative one week prior.

¶1 Child died at the age of fifty-six hours. Polycystic kidney disease. No syphilis.

N.D.—Note done.

### Massive Arsenotherapy Results

Table I shows that, in the total of forty pregnant women treated, thirty-eight of their infants have been checked since delivery. All were normal term deliveries. No stillbirths or abortions occurred.

There were four patients who had dark-field positive primary syphilis; two cases were in the first trimester of pregnancy, and one each in the second

\*With the eight-day treatment 20 per cent had nausea and vomiting, 20 per cent secondary fever, and 20 per cent toxicoderma. All the reactions were minor.

per cent misearriages. Ten per cent of the live births had positive Wassermann serologic tests at the end of four months; a good indication that they had syphilis.

Dippel<sup>5</sup> autopsied 68 fetuses of adjudged nonsyphilitic women and 67 fetuses of syphilitic women. Spirochetes were found in the fetal organs of 23.9 per cent of the fetuses of syphilitic mothers, and none in the other group. Spirochetes were not found in any fetus prior to the eighteenth week of gestation. The highest incidence of syphilis was found in the fetuses (66.7 per cent) at the twenty-sixth week. Dippel concludes that antisyphilitic therapy should be started before the eighteenth week of gestation in order to prevent the invasion of the fetus by spirochetes. He also presents important evidence to show that Langhan's layer of the chorionic epithelium affords appreciable protection to the fetus against invasion by the *Spirochaeta pallida*, until it becomes thinned sometime during the sixteenth or eighteenth week of pregnancy.

In 1942, Sadusk and Shaffer<sup>6</sup> first reported using massive arsenotherapy in the treatment of early syphilis shortly before and shortly after the beginning of pregnancy. The patients received the five-day drip method of Hyman, Chargin, and Leifer, consisting of the administration of 1,200 mg. of mapharsen by intravenous drip over a period of five days. Two of the four reported cases became pregnant, two and three months respectively, following completion of treatment. Both women remained seronegative and delivered normal seronegative babies, which remained negative for six months. The other two cases were pregnant five and fourteen weeks respectively at the time of treatment, but unfortunately no follow-up report on these pregnancies is given.

In 1943, Rattner<sup>7</sup> reported the use of the five-day arsenic rapid treatment in 27 cases of pregnant women with syphilis. Eight of the patients had early latent syphilis, the rest early infectious syphilis. The majority were five or more months pregnant, and none had received previous antisyphilitic treatment. The results show that twenty-five of these women delivered normal babies. One was apparently reinfected just prior to delivery, and one could not be followed.

Speiser, Wexler, Thomas, and Asher<sup>8</sup> reported their results on 43 pregnant women treated for syphilis with rapid mapharsen therapy. One death from arsenical arsenotherapy occurred in this group. Thirty patients who had early infectious syphilis were kept under observation. Their probable good results were 85 per cent.

In January, 1942, we began the treatment of syphilis in pregnant women with massive arsenotherapy. The first method used followed that outlined by Hyman, Chargin, Rice, and Leifer,<sup>9</sup> using 240 mg. of mapharsen in 2,000 c.e. of 5 per cent glucose given intravenously daily for five consecutive days. The mapharsen glucose solution was given at the rate of approximately 4 c.e. per minute, and took from eight to ten hours for completion of the daily dose. A total of 1,200 mg. of mapharsen was given to each patient. In addition to the mapharsen, each patient received 130 mg. of bismuth subsalicylate in oil intramuscularly at the start, and again at the completion of treatment, making a total of 260 mg. of bismuth. Twenty-nine women with early syphilis and pregnancy, and one woman with congenital syphilis and pregnancy were treated by this method.

In January, 1945, we discontinued the use of the five-day massive arsenotherapy because of its toxicity<sup>10\*</sup> and began a modification of it which, we be-

\*Toxic reactions were moderately severe with the five-day treatment. Sixty per cent had nausea and vomiting on the first day of treatment. It rarely continued into the second day of treatment. Thirteen per cent had primary fever, 10 per cent secondary fever, 3.3 per cent toxicodermas, and 1.3 per cent (one case) had an arsenical encephalopathy.

All six of these women received bismuth subsalicylate in oil, at weekly intervals from the time rapid massive arsenotherapy was discontinued until delivery. Two of the mothers reverted to seronegativity and remained negative for two years. Four have shown a gradual drop in serologic titer and, when last checked, two to three years after treatment, were positive at 4 units only. This type of slow serologic titer change, or even serologic titer fastness is not unusual in latent syphilis, even after massive arsenotherapy.

One woman, who had congenital syphilis and acute interstitial keratitis, and who was in the second trimester of her pregnancy, was treated with the five-day treatment. Her serologic titer was 80 units. The child's development was normal. The serologic test remained negative throughout three months of observation. The mother reverted to negativity within three months and remained seronegative throughout the fourteen months observed.

Three women became pregnant the second time. None was given treatment after the original massive arsenotherapy. Previously two of the women had early secondary, and the third early latent syphilis. One delivered two years and eight months after treatment, the other two, twenty-one months after treatment. Two infants were checked at the end of three months. Both were clinically and serologically negative. The serologic test on both mother and third infant was negative at birth. The infant has not been checked since.

The above data are summarized in Table I.

### Discussion

The diagnosis of congenital syphilis may be made certain by a dark-field examination of serum from the umbilical vein or infant skin. However, other less accurate procedures are usually used, such as the examination of the placenta for gross pathologic as well as microscopic changes; the cord blood serologic test; an x-ray of the infant for periosteal and bone changes, and the common physical signs of congenital syphilis. Unfortunately the two most common procedures used for the diagnosis of prenatal syphilis are the cord blood serologic test and the pathologic examination of the placenta. Both of these procedures are valueless in making such a diagnosis, and may even lead to erroneous conclusions.

Faber and Black,<sup>11</sup> Christie,<sup>12</sup> and others have demonstrated that maternal syphilitic reagin may appear in the blood of nonsyphilitic infants in titer equal to or lower than that in the mothers' blood. A positive serologic test obtained from cord blood may be then only an index of the mothers' reagin and not the infants'. Maternal reagin remains in the infants' blood for varying lengths of time. It usually disappears during the first month of life, but has been demonstrated in measurable quantities for as long as seventy days. For unknown reasons, cord bloods done by complement fixation tests are more prone to be positive than when done by flocculation tests.<sup>13</sup>

Ingraham<sup>14</sup> has shown that eighty-seven such infants with initially positive serologic tests, which subsequently reverted to negative, showed no evidence of late congenital syphilis six years later. Table I shows that three infants in this series had positive cord blood tests. All became negative in three months, without treatment.

If a child is infected in utero or in the birth canal, the cord blood can be either negative or positive. If negative, the blood serologic test will become positive sometime before the twelfth week as the infant develops its own syph-

and third trimester of their pregnancy. The mothers' serologic tests varied from 0 to 8 units. One baby was followed for three months, one for twelve months, and the other two for eighteen months. All remained serologically and clinically negative. The mothers returned to seronegativity within two months after treatment, and remained seronegative throughout the next ten to eighteen months.

There were twenty-seven cases of early secondary syphilis. None had received previous therapy and all were seropositive and dark-field positive, with serologic titers varying from 40 to 320 units.

Six patients were in the first trimester of pregnancy. Four of their babies were followed from three to eight months, and remained seronegative and normal infants. One child could not be followed; one child died at the age of seven days. An autopsy diagnosis was made of virus enteritis without evidence of syphilis.

Fourteen patients were in the second trimester of pregnancy. Eleven children of this group were followed from three to twenty-seven months, and all remained serologically and clinically negative. Two children were not followed. One died at the age of three months of an unknown cause, but without evidence of syphilis. A serologic test on this infant one week prior to death was negative. It is interesting to note that three of the mothers had threatened abortions with severe cramps and spotting on admission. They were immediately treated with massive arsenotherapy and sedation. After the third day of treatment the spotting and cramps disappeared. Delivery was at term.

In the third trimester of pregnancy, seven women were treated. Four infants remained negative and normal throughout a period of three to twenty-four months. One child died two and one-half days after birth. An autopsy showed polycystic kidneys, but no evidence of syphilis. Two children could not be checked after birth. The twenty-seven mothers of these babies became seronegative at the end of eight months and remained clinically and serologically negative throughout a period of eight to twenty-seven months.

There were two patients who had late secondary syphilis. Both were dark-field positive and the serologic titers were 80 and 560 units. One woman was in the second trimester of pregnancy when treatment was instituted. Her child's development was normal, and the infant remained seronegative throughout a period of eight months. The second woman was nearing term when treatment was begun. She delivered the day following completion of treatment. There were no signs of syphilis in the baby. In two weeks the infant's blood test was negative and remained repeatedly negative through twenty-four months. The child's development was normal. Both mothers reverted to seronegativity at the end of five months and remained seronegative through twelve and twenty-seven months, respectively.

There were six women who had early latent syphilis (syphilis less than four years old) and pregnancy. One woman had previously received a few bismuth injections. The other five were untreated.

One woman was in the first trimester of pregnancy. Her baby developed normally and was seronegative four months later.

There were four women in the second trimester of pregnancy. Their serologic titers ranged from 40 to 120 units. Five infants resulted from these four pregnancies. All babies developed normally. All remained seronegative throughout a period of eight to twenty-one months.

One woman was in the third trimester of pregnancy and had a serologic titer of 80 units. Her baby was seronegative at the end of three months and remained seronegative for six months.

evidence of syphilis. The third infant was not autopsied. It had no serologic or clinical evidence of syphilis at three months of age. Thirty-three infants developed normally and remained seronegative. Three mothers became pregnant a second time. None was again treated. Two infants, born of these mothers, were observed for three months and remained serologically and clinically negative.

3. All mothers with primary or secondary syphilis returned to seronegativity and remained so through at least two years.

4. There were no abortions, miscarriages, or stillbirths in this group.

5. The diagnosis of congenital syphilis is discussed.

6. Massive arsenotherapy offers the pregnant patient with *early* syphilis a probable cure of her syphilis and a noninfected baby.

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ilitic reagin. If positive, it may become negative, then again positive. This is due initially to the presence of the mother's reagin, which at first causes the positive reaction. The disappearance of the mother's reagin leads to a short period of negativity. Later the child develops syphilitic reagin from its own infection and the serologic test is again positive. These facts show that an infant with a positive cord blood serologic test may ultimately prove to be non-syphilitic. A child with a negative cord blood serologic test may later develop congenital syphilis. The serologic test on cord blood is evidently worthless as a working tool for the diagnosis of congenital syphilis. If positive, it may lead to unnecessary treatment of a healthy child; if negative, it may give a false security, which delays necessary treatment and eventual stigmatization of the child. Three infants reported in this series had positive cord blood serologic tests. All became negative without treatment for six, eight, and twenty-four months. See Table I.

The placenta has long been examined for evidence of syphilis. Its value as a diagnostic aid in identifying congenital syphilis in a living child has been shown to be worthless by Dill, Stander, and Isenhour.<sup>15</sup> In none of his cases of congenital syphilis was the placenta positive pathologically. Dill has shown that most infected placentas are found in macerated fetuses, which lead to abortion and not viable infants. He has also drawn attention to similar vascular abnormalities in the placenta due to causes other than syphilis.

It would seem, then, that the two special types of examination most commonly used for the diagnosis of congenital syphilis should both be discarded. In the absence of the physical signs of syphilis, diagnosis should depend upon a dark-field examination of cord serum, x-ray change of the periosteum and bones, and a blood quantitative serologic test done eight to twelve weeks after birth.

Massive arsenotherapy offers a rapid and highly efficient method for treating early syphilis associated with pregnancy. It is our opinion that many of the patients with early syphilis treated by this method are not only serologically, but biologically, cured. We believe this applies to the fetus in utero as well as to the mother. Even in the last trimester of pregnancy, when there is insufficient time for routine treatment, none of our infants had syphilis. There were no abortions or stillbirths in forty patients treated. Two threatened abortions were alleviated. The reactions due to the treatment are appreciable. Hemorrhagic encephalitis may even be a fatal complication. However, no other form of antisymphilitic treatment has offered such good results to date. Penicillin will probably be as efficacious and much less hazardous.

### Summary and Conclusions

1. Forty women with syphilis, complicated by pregnancy, were treated with massive mapharsen therapy.

2. Thirty-three infants born of these mothers were kept under observation through at least three months of age. Five could not be followed. Three infants died. Two were autopsied and had neither clinical, serologic, nor pathologic

dren being 2.7. Twenty per cent of the patients had never been pregnant, whereas another fourteen per cent had had an average number of 1.9 abortions. The average stay in the hospital was 20.9 days. The average stay preoperatively was 8.9 days; postoperatively, 12.0 days.

Twenty-three per cent of the patients had undergone previous major surgery. Morbidity and mortality in the present surgery were not appreciably affected by this previous surgery.

At this point previous errors in doing "incomplete surgery" should be pointed out and stressed. There were sixty-three patients (16 per cent) that had undergone previous pelvic surgery. Twenty-one patients had undergone previous tubal ligation for sterilization purposes. Now these patients complained of menometrorrhagia, backache, pelvic pain, etc., to the extent that they were chronic invalids requiring further surgery, and really adequate sterilization consisting of hysterectomy and bilateral salpingectomy. Eighteen of these twenty-one patients had varicosities in the broad ligaments at surgery. Time and again this situation has presented itself. It cannot be stressed too sharply that when an abdomen is opened principally for sterilization purposes, an adequate sterilization should be carried out. This does not imply that tubal sterilization does not have its place, but its successful utilization is rapidly decreasing. In a period of three years at the Los Angeles County Hospital there have been six incidences of pregnancy following tubal "sterilization."

Thirty-one patients had further incomplete surgery consisting of unilateral salpingectomy and/or oophorectomy, etc., for inflammatory disease. Boyd<sup>1</sup> states that a specific salpingitis is practically "always bilateral." Curtis<sup>2</sup> states that a "specific salpingitis is almost invariably bilateral." Other writers agree that if one tube is involved, both tubes are practically always involved. Wharton, Curtis, and Henrikssen all advise removal of both tubes and a hysterectomy for all operations for salpingitis. Emergency surgical procedures, such as ectopic pregnancy, appendectomy, ruptured pyosalpinx, or simple drainage of pelvic abscesses are exceptions, of course. Incomplete surgery in pelvic inflammatory disease will often terminate in ectopic pregnancy, pyosalpinx, and further surgery.

Incomplete surgery consisting of bilateral salpingectomy without hysterectomy accounted for several patients with uterine hemorrhage requiring further surgery. Too often the uterus is the site of a concomitant metritis, or is subject to aberrant hormonal stimulation following bilateral salpingectomy.

TABLE II. INDICATIONS

	PELVIC INFLAMMATORY DISEASE		FIBROID		RELAXATION	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Pain	217	55	14	3.6	0	0
Bleeding	99	25	77	19.7	2	0.5
Tumor (pressure)	8	2.0	55	14.1	0	0
Discharge	77	19.7	28	7.1	4	1.0
"Something falling out," and so forth	0	0	0	0	37	9.5

Subjectively, pain and hemorrhage either individually or collectively were the presenting symptoms in 81 per cent (316) of the patients. The presence of a "tumor" or/and pressure symptoms brought another 14 per cent (55 patients) to the hospital. Nine and five-tenths per cent (37) came because of prolapse, "womb falling out," "something coming out," and so forth. Miscellaneous complaints brought in 37 patients, or about 10 per cent.

# CRITICAL STUDY OF 390 MAJOR GYNECOLOGIC SURGICAL PROCEDURES\*

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IN ORDER to insure the best possible medical and surgical care for patients under professional treatment, errors in judgment must be searched for and corrected. A very meticulous and painstaking search must be made, for a patient's life may depend on a single laboratory or physical finding. With that thought in mind, a critical analysis of 390 major gynecologic surgical procedures has been undertaken. These patients were operated upon at the Los Angeles County Hospital in 1943 and 1944. For the most part, the patients were taken from the gynecologic service of Dr. Roy Fallas, senior attending physician.

TABLE I

OPERATION	INTERN		RESIDENT		ATTENDING STAFF	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Subtotal hysterectomy	19		26		10	
Subtotal hysterectomy plus	15		183		27	
Total abdominal hysterectomy	0		35		4	
Total hysterectomy plus	0		4		2	
Vaginal hysterectomy	0		14		5	
Adnexal surgery	6		22		3	
Miscellaneous	0		11		4	
Totals	40	10.3	295	75.6	55	13.1

The operators were the intern on the service, the resident physician, and the junior attending or senior attending physician. Table I shows the distribution of surgical procedures and operators.

From this table it will be seen that the resident physician does the major part of the surgery. He is at all times under the direction and supervision of the attending staff.

During the period of one year covered by this study there were a total of 801 admissions to the Los Angeles County Hospital gynecologic service, from which the 390 major operative patients were taken. Therefore, 48.6 per cent of the patients admitted to the hospital from the diagnostic clinic and main admitting room underwent major surgery. It has been the policy of the admitting services of this hospital during the war emergency to admit only patients requiring emergency care. Therefore the surgical incidence would be necessarily high.

## Statistics

The average age of the patients undergoing surgery was 34.4 years. Of this group of women 66 per cent, or 257, were parous—the average number of chil-

\*Presented before the Los Angeles Obstetrical and Gynecological Society, Dec. 11, 1945, and the Los Angeles County Surgical Society, April 12, 1946.



### Diagnosis

A correct diagnosis preoperatively was made in 69 per cent of the patients. Each patient before surgery was examined by the intern, resident, and attending physician. The diagnosis was partially correct in 16 per cent of the patients. In 15 per cent the diagnosis was erroneous.

### Surgery

Surgical procedures carried out are shown in Table IV.

TABLE IV

OPERATION	NUMBER	PER CENT	STAY IN HOSPITAL POSTOPER- ATIVELY	MORBIDITY (PER CENT)	MORTALITY	OPERATING TIME IN MINUTES
Subtotal hysterectomy	55.0	14.1	10.2	26	0	54
Subtotal hysterectomy plus	225	57.7	10.4	36	1.0	66
Total abdominal hys- terectomy	39	10.0	12.2	24	0	68
Total abdominal hys- terectomy plus	6	1.5	12.7	30	0	72
Vaginal hysterectomy	19	5.0	13.1	54	1.0	78
Adnexal surgery	31	8.0	9.8	38	1.0	37
Miscellaneous	15	3.8	10.5	31	1.0	47
						(Average 60 minutes)

The relative infrequency of total abdominal hysterectomy and vaginal hysterectomy is explained by several reasons. Total abdominal hysterectomy is not an easy procedure in the most experienced operators' hands. In the presence of such advanced stages of pathologic disease as is seen in such a series, particularly in the pelvic inflammatory disease cases, it is felt that the morbidity and mortality figures would prohibit the use of the total hysterectomy, except in these cases where there is an absolute indication for the extirpation of the cervix also. Extensive cellular exudates and vascularity with dense adhesions make total hysterectomy difficult and dangerous in these cases.

We will not attempt to evaluate the total versus subtotal arguments, as that is not within the scope of this paper.

The average operating time from skin incision to complete skin closure was sixty minutes. The shortest operation was twelve minutes on a ruptured ectopic, to the longest procedure of one hundred thirty-five minutes on anterior and posterior repair and subtotal hysterectomy. The latter procedure was too much surgery for one sitting.

Vaginal hysterectomy was not done except in the presence of prolapse of the uterus. Various interpositional and complicated procedures from below were not attempted.

### Anesthesia

Spinal anesthesia was the anesthetic agent of choice. Other types of anesthesia are shown in Table V.

TABLE V

Spinal	79%
Cyclopropane	12%
Ether	5%
Curare	1%
Caudal, miscellaneous	3%

Objectively, pelvic inflammatory disease was the principal diagnosis in 43 per cent, or in 168 patients. Fibromyomata uteri with and without pelvic inflammatory disease was the principal diagnosis in 38 per cent, or in 149 patients. Uterine hemorrhage, shock, acute pelvic pain, etc., account for the additional 19 per cent, or 73 patients.

As pelvic inflammatory disease was the principal indication for surgery, it will be seen that the criteria for surgery in inflammatory disease are rather uniform. If the disease is persistent to the point of making the patient a chronic invalid, surgery is advised. Repeated, crippling, incapacitating recurrences of pelvic pain, uterine bleeding, chills, and fever to the point of complete exhaustion of the patient are evidence enough for surgery. Conservative medical treatment should be faithfully and patiently carried out. Most often pelvic inflammatory disease will resolve under a careful medical regime.

TABLE III. PATHOLOGY (POSTOPERATIVE)

Pelvic inflammatory disease		242
Fibromyoma		167
Pelvic inflammatory disease plus fibromyoma		137
Ovarian cystoma		47
Retention cysts	24	
Papillary serous	9	
Dermoid	7	
Pseudomucinous	4	
Miscellaneous	3	
Ectopic		37
Endometriosis		12
Carcinoma of the fundus		10
Sarcoma		3
Endometrial	1	
Botryoides	1	
Leiomyosarcoma	1	
Actinomycosis		1
Tuberculous salpingitis		1
Miscellaneous		9

Pelvic inflammatory disease was the chief pathologic finding, as shown in Table III, and in this hospital represents the ultimate and usually the most advanced stage of pathogenesis. Thirty-four per cent of the patients with pelvic inflammatory disease had tuboovarian abscess, one or two, at the time of surgery. In all types of pathology seen in an institution such as this, the disease process has usually run its course. The state of exhaustion, malnutrition, and degree of pathology seen in these patients is not usually seen in private patients.

One interesting observation is the twelve cases of endometriosis in a series of 390 gynecologic laparotomies for an incidence of 3.0 per cent. It was recently shown that there is a much greater percentage of endometriosis in private practice among patients in the higher social and economic levels than in the charity patients in such an institution as the Los Angeles County Hospital. The incidence among private patients is quoted from 10 per cent to 32.2 per cent by various authors. Dr. Roy Fallas<sup>3</sup> reports an incidence of 37 per cent in his last series of 100 laparotomies. Reasons for this variance have been explained by delay in childbearing or years and years of menstruation without interruption (Meigs<sup>4</sup>). Use of contraceptive devices is also a point of contention.

Other interesting reports from the pathologist are: a case of sarcoma botryoides—the grapelike sarcoma of the cervix, corpus in children or infants, and, in this instance, in a 52-year-old Ethiopian woman. One case of endometrial sarcoma is reported. One case of leiomyosarcoma was found on examination. One case of pelvic actinomycosis is reported, which responded to penicillin, surgery, and postoperative irradiation.

TABLE VI. MORBIDITY

CRITERIA	CRITERIA FULFILLED (PER CENT)	CRITERIA NOT FUL- FILLED (PER CENT)
As a whole	18	47
Cautery of cervix	26	69
Hemoglobin 60 per cent. White blood cells 7 to 10,000, with 60 to 80 per cent polymorpho-nuclears	17	63
Sedimentation rate, 20 mm. or less	27	57
Normal urine	13	74
Normal physical	30	38

It is plain that close attention must be paid to every detail before a patient is subjected to major surgery. Cautery to the cervix, a normal urine and blood work are among the more essential preoperative musts.

Causes of morbidity in so far as can be determined are listed in Table VII.

TABLE VII. PERCENTAGE OF DISTRIBUTION OF MORBID PATIENTS

CAUSE OF MORBIDITY	TOTAL ABDOMINAL HYSTERECTOMY (PER CENT)	SUBTOTAL HYSTERECTOMY (PER CENT)	VAGINAL HYSTERECTOMY (PER CENT)
Genitourinary	33	37	68
Pulmonary	22	23	0
Undetermined	39	30	20
Sepsis	2	7	12
Thrombophlebitis	1	2	0
Transfusion reaction	1	0	0
Miscellaneous	2	1	0

### Operative Accidents

The urinary bladder was not knowingly injured in this series. The large and small bowels were inadvertently opened on one occasion in the same patient. Freeing extensive pelvic adhesions resulted in small multiple perforations in the small bowel and one larger perforation in the sigmoid. Six inches of small bowel were resected—and end-to-end anastomosis was done. The sigmoid was closed and a protecting simple loop colostomy was done above the defect. The patient recovered following closure of the colostomy.

There were no further operative accidents to our knowledge.

### Appendectomy

Routine appendectomy was not done in this series. This was discussed with the patient preoperatively. The great majority requested removal. At operation, appendectomy was done if there were no contraindication such as further prolonging an already long period on the operating table, or as in ruptured ectopics, etc.

Twenty-one per cent of the patients, or 92, had already undergone appendectomy. A further 19 per cent, or 75 patients, had only plastic surgery or emergency surgery, such as ruptured ectopic, etc. Of the remainder, appendectomy was done in 60.4 per cent, or in 139 patients.

There were no unusual complications in the appendectomy group, such as wound infection, etc. The morbidity in the group that had appendectomy was 34.6 per cent, or 48 patients, slightly higher than the group as a whole—34 per cent. In the patients that did not have appendectomy, the morbidity was 29 per cent, or 84 patients, which is slightly less than the general group of morbidity, and noticeably less than the 34.6 per cent in the group that had appendectomy.

There were no deaths or unusually severe accidents attributed to the anesthetic agent.

### Morbidity

A temperature of 100.4° F. or more for two days, excluding the first post-operative day, was considered as a morbidity in this series. The morbidity incidence with these criteria was 20 per cent, or 78 patients. To emphasize contrast, morbidity, as shown in the tables and as otherwise quoted here, is based on a temperature of 100° F. or more on any *one* day, representing a morbidity of 34 per cent, or 133 patients.

Polak and Tollefson<sup>5</sup> have enumerated various criteria for lowering the incidence of morbidity and mortality in elective cesarean section. If these criteria are followed in all pelvic surgery, better results will follow. These criteria are:

1. A complete history and general physical examination.
2. A leucocyte count of between 7,000 and 10,000.
3. A polymorphonuclear percentage of from 65 to 80.
4. A hemoglobin of at least 60 per cent.
5. A sedimentation time of ninety minutes or more.
6. A normal urinalysis, and an adequate kidney function.
7. A temperature of 98.6° F. for at least forty-eight hours before operation.
8. A systolic blood pressure between 110 and 150.
9. A negative Wassermann test, and finally, that all elective preoperative patients have rest in bed in the hospital for a period of at least forty-eight hours, during which time the intake of fluids, water, milk, etc., must be at least two and one-half quarts per day, while the usual sugar intake of the individual must be at least quadrupled.

There have been other points of interest raised with regard to morbidity and mortality. Cashman and Fran<sup>6</sup> have shown that when cauterization of the cervix was done, particularly in subtotal hysterectomy, mortality was lowered from 6.5 per cent to 1.1 per cent in a series of about 1,500 cases. Also, deep cauterization of the cervix was shown by Cashman to be an effective method of preventing carcinoma of the cervix in a series of 10,000 cases. In this small series, cauterization of the cervix was thoroughly done in 316 (81 per cent) of the cases. In these 316 cases there were 82 morbidities, an incidence of 26 per cent. In the 74 patients (19 per cent) that did not receive the cautery to the cervix, there were 51 morbid patients, for an incidence of 69 per cent. Comparing a morbidity incidence of 26 per cent with the cautery used to a morbidity of 69 per cent with the cautery not used, it can readily be understood why thorough cauterization from below is a large factor in morbidity, mortality, and possibly incidence of cervical carcinoma.

Too much stress cannot be laid upon an absolutely afebrile period of at least one week before surgery, particularly in pelvic inflammatory disease. There was such a small percentage of the patients febrile before surgery that the value of having the preoperative period clear of fever cannot be clearly indicated. It is of utmost importance, however, and cannot be emphasized too much.

Considering Polak's and Tollefson's criteria as a unit, and adding cautery to the cervix, it is seen that 171 patients fulfilled all the requirements for surgery. In this group of patients, 29 were morbid for a percentage of 18 per cent. In further investigating, it is seen that 219 patients did not fulfill the requirements. Out of this group there were 105 morbid patients for a percentage of 47 per cent, more than twice as great a percentage of morbidity as shown in this carefully prepared group.

Various authors have mentioned what they consider as the more important criteria for operability of a patient. Considering these criteria in groups, it is seen that there is varying significance.

cauterization of the cervix so decidedly affects morbidity is not exactly known. Perhaps it is a sterilization of the cervix and endocervix. Perhaps it is a sealing of the lymphatics and blood vessels to prevent spread of infection into parametrial tissue.

Particular stress is to be placed upon "incomplete surgery," especially in pelvic inflammatory disease. Too many practicing gynecologists have reopened abdomens with lower midline incisions that have had one tube or a part of one ovary, etc., removed at a previous pelvic laparotomy. It is desired that more complete and satisfying surgery be done if the abdomen is opened at all. If the chronic inflammatory disease is serious enough to warrant abdominal exploration, hysterectomy and bilateral salpingectomy should be done if diagnosis is correct.

The total morbidity was found to be 20 per cent—mortality 1.03 per cent. Cautery to the cervix, a normal blood count, and urine are found to be very important to the patients' welfare. Appendectomy is shown to raise morbidity slightly.

### Conclusions and Summary

1. More attention should be paid to factual information pertaining to the patients' preoperative condition before major surgery.

2. The type of operation performed must not be made a routine. Every patient must have what is the best surgery possible under the sustaining conditions.

3. We learn not by discussing successes, but by carefully evaluating mistakes and then acting accordingly.

4. If the abdomen is opened, more complete surgery should be done.

5. Complete and careful evaluation of kidney function must be carried out in patients undergoing extensive vaginal plastic procedures.

I wish gratefully to acknowledge the valuable suggestions given to me by Dr. Roy Fallas and Dr. D. G. Tollefson in the preparation of this publication.

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### Mortality

There were four operative mortalities in the entire series—an incidence of 1.03 per cent.

TABLE VIII. MORTALITY

AGE	CRITERIA FULFILLED	PREOPERATIVE DIAGNOSIS	SURGERY	CAUSE OF DEATH	OPERATOR
37	No	Pelvic inflammatory disease	Subtotal hysterectomy, bilateral salpingectomy, appendectomy	General peritonitis paralytic ileus, (autopsy)	Resident
45	No	Ovarian cyst with hemorrhage	Closure perforation, diverticulum drainage	General peritonitis (autopsy)	Attending
54	No	Ovarian cyst	Left oophorectomy	Coronary occlusion	Resident
43	No	Procidentia cystocele—rectocele	Anterior-posterior repair, vaginal hysterectomy	Uremia, chronic pyelonephritis (autopsy)	Attending

In no one case were the operative criteria, as previously outlined, fulfilled. In the first case the sedimentation rate was 32, despite seven weeks absolute rest in bed. She died on the eighth postoperative day from causes as above outlined. This death could probably have been prevented had the patient waited in bed. The responsibility rests with the doctor. An autopsy was done.

The second case had a large papillary serous cystadenoma which was causing dyspnea and other pressure symptoms. Her blood pressure was 210/115. A spinal anesthetic was given, consisting of 100 mg. of procaine and 2 mg. of nupercaine. The blood pressure dropped to 160/100 at its lowest point during the surgery. She died suddenly on the third postoperative day with what was clinically diagnosed as coronary occlusion. Perhaps drop ether should have been used—certainly not the nupercaine.

The third patient died of a general peritonitis secondary to a perforated diverticulum and pelvic abscess. She was an obese Caucasian woman with a pelvic mass. Her white blood count was 12,700 with 82 per cent polymorphonuclears shortly before surgery. The possibility of pelvic abscess from perforated diverticulum was discussed. Proctoscopy was advised but not carried out. This death at least partially rests on the doctor's shoulders. It is easy to make diagnostic errors—but all diagnostic means at hand should be made use of, particularly in a poor risk patient.

The last patient died on the sixth postoperative day of uremia following anterior and posterior repair and vaginal hysterectomy. The patient had a blood pressure of 160/100 and a two plus urinary albumin before surgery. Kidney function was not evaluated. The patient was in the hospital for four days before surgery. The exciting cause of death is the responsibility of the doctor.

### Comment

In any major surgical procedure, there are a multitude of important factors to be considered. The age of the patient, the state of nutrition, the preoperative diagnosis, the innate general resistance of the patient for which there are no good criteria, etc. However, there are some factual criteria upon which we can rely. These criteria have been outlined and their relative importance shown in this small series. An additional factor, cauterization of the cervix, is found to be a very important factor in preventing morbidity. The mechanism by which

and urinalysis remained normal. A diagnosis of hydramnios was made. Roentgenographie examination disclosed that the outline of the fetal skeleton could be distinctly visualized. The head was presenting and the small parts were in the right side of the abdomen. There was no apparent disproportion between the fetal skull and the maternal pelvis. The uterus was markedly enlarged, consistent with hydramnios.

Ammonium ehloride was prescribed at that time. The dosage was 90 grains daily, administered in enteric-coated tablets. Four tablets ( $7\frac{1}{2}$  grains) were given after each meal for seven days, beginning on November 15. Ten days later, the abdomen was less tense and had the appearance of a seven and one-half months' pregnancy. The weight was reduced to 138 pounds. The patient was observed at weekly intervals thereafter; blood pressure and urine did not change. The urinary output was in excess of the intake.

On Jan. 13, 1941, the patient entered the hospital at 2:00 A.M. After an enema, labor progressed rapidly, with delivery by perineal forceps at 4:31 A.M. A normal male infant weighing 7 pounds was born. Both mother and child are normal in every respect at the present time, more than four years later.

CASE 2.—A white woman, aged 24 years, para 0, gravida i, whose average weight had been 105 pounds, experienced her last menstrual period on July 7, 1943. Confinement was expected April 21, 1944. The menarche had occurred at the age of 13, the cycle was twenty-eight days, and menstrual flow lasted six days. The flow was moderate, and the patient had had no clots and no pain. Aside from several orthopedic operations for a foot deformity, she had been in good health. The uterus was slightly enlarged, in good position, and there was slight softening of the body, with a presumptive diagnosis of pregnancy on her first visit, Sept. 10, 1943. The remainder of the physical examination revealed essentially normal findings. Pelvic measurements were within normal limits. Urinalysis and serologic tests were negative, and the blood pressure was 120/80.

When the patient was seen on Dec. 14, 1943, during the fifth month of pregnancy, the uterus was enlarged far beyond the normal growth at this stage. The uterus was about 5.5 centimeters above the umbilicus and was tense. The fetus could be palpated, but appeared small. The blood pressure was 115/80, and the patient weighed 121 pounds. Urinalysis was within normal limits. Hydramnios was suspected and a roentgenographie examination was carried out. This revealed a five and one-half months' fetus with a breech presentation in both the anteroposterior and the lateral views. The uterus was enlarged out of proportion to the size of the fetus, reaching to the level of the lower border of the second lumbar vertebra, indicative of hydramnios. One week later (Dec. 24, 1943), the uterus was palpated about 6 centimeters above the umbilicus, and was extremely tense. A salt-free diet with a saline purgative was prescribed. On Dec. 30, 1943, the uterus was still very tense, and the size was fractionally increased. On January 6, the patient's weight was 124 pounds, the blood pressure 110/80, and the urine showed 1 plus albumin. A week later, the uterus was over 7 centimeters above the umbilicus, and urine albumin had increased to 2 plus. The blood pressure was 120/85, and weight was  $123\frac{1}{4}$  pounds.

At this time the patient received 15 grains of ammonium ehloride (two enteric-coated tablets per dose) every three hours, i.e., about 75 grains a day. This produced marked frequency of urination. The ammonium ehloride was discontinued a week later (Jan. 20, 1944), at which time the patient's weight was 123 pounds, the blood pressure was 120/80, and urinalysis yielded negative findings. The height of the uterus was markedly decreased to within 2 centimeters above the umbilicus. The fetal parts could be palpated well, and the head was presenting.

The patient was seen every two weeks thereafter. Her progress was entirely normal. The blood pressure remained at 120/80; the weight increased gradually

# SUCCESSFUL TREATMENT OF HYDRAMNIOS WITH AMMONIUM CHLORIDE

## A Preliminary Report

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**H**YDRAMNIOS constitutes a serious obstetric problem for which there has been no adequate treatment. The usual procedure in such cases is watchful waiting until the condition has progressed to a stage where intervention cannot be avoided. Since, in the majority of patients with hydramnios, this condition occurs in the sixth to eighth month of pregnancy, it is frequently impossible to bring about delivery of a viable fetus. A large proportion of these offspring are monsters, and the others are likely to have some less severe physical or mental handicap. Hence the prognosis generally, so far as the child is concerned, is very poor, both for life and for health.

In view of these facts, we have investigated the properties and effects of various diuretics in the hope that one could be found which might be used in hydramnios with beneficial results both for mother and for child. Ammonium chloride was selected, and in cases of hydramnios in which it has been used, it has brought prompt relief to the mothers, with no toxic manifestations; and they have been able to deliver viable, normal fetuses.

Two cases can be reported in detail at this time, since one of us (A. A. A.) is on active military service, and hence has no access to records of several patients treated successfully at the Boston City Hospital. These patients with hydramnios were treated in the sixth month of pregnancy, and they were delivered of normal infants at term.

CASE 1.—A white woman, aged 23 years, para 0, gravida i, had had an average weight of 119 pounds. Her last menstrual period occurred April 8, 1940, and confinement was expected Jan. 15, 1941. During the first trimester she had experienced mild nausea and vomiting. Physical examination at her visit on July 16, 1940, revealed no abnormal findings. The uterus was anteriorly situated, symmetrical, and enlarged to a size consistent with a three months' pregnancy. The blood pressure was 120/80, and the pulse rate was 80 per minute. Urinalysis and vaginal smear were normal.

On Oct. 7, 1940, the patient's weight was 132 pounds. This was regarded as excessive, and a salt-free diet was prescribed. Three weeks later (October 28) she appeared and felt very well. She had experienced no nausea or vomiting, bowel evacuations were normal and regular, and she had no edema. The patient weighed 138½ pounds. Her blood pressure was 120/80. The fetus was active. However, at this time, abdominal enlargement was comparable with that of an eight months' pregnancy. The question was raised as to whether there might be twins to account for the enlargement, but only one fetus was palpated and only one fetal heartbeat was heard. Hydramnios was suspected because of the tenseness of the abdomen.

On Nov. 12, 1940, the uterus still was as large as that of an eight months' pregnancy, and the patient weighed 143 pounds. The abdomen was tense, but there was no evidence of dependent edema. The blood pressure had not changed,

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## SARCOMA OF THE VAGINA\*

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THE presenee of primary sareoma of the vagina is fortunately rare, for it carries with it a most grave prognosis. We are presenting at this time the only two cases of this type found at the University of Maryland during the past ten years, and during which time there were 8,589 gynecologic admissions. This incidence seems to tally fairly well with that reported by Lynch from the University of California, where he found one case of vaginal sarcoma among the last 4,000 gynecologic cases.

In 1935, McFarland presented a most complete and exhaustive treatise on the dysontogenetic and mixed tumors of the urogenital region. In this he made some reflections on the nature of sarcoma which are well worth quoting. The term, sarcoma, derived from the Greek, literally means "fleshy swelling" or "lump of flesh." The term, though used generally, is given a different interpretation by clinicians and pathologists. However, both groups will agree on the following fundamental principles: (1) sarcoma is a malignant tumor; (2) it occurs chiefly in the young; (3) it consists essentially of cells; (4) the cells are of mesoblastic origin; (5) the cells are of embryonal type; (6) they represent the early form of the connective tissues.

Many of the vaginal sarcomas that have been reported in the literature arise in childhood and are most commonly of the botryoid type. The first case report of this tumor was made by Gersant in 1854. In 1911 McFarland reviewed the literature and tabulated 44 cases of vaginal sarcoma in children, 34 of which were botryoid, and the remaining 10 were classified as miscellaneous; 86 per cent of these 44 cases occurred during the first three years of life, and the remaining were found before the sixth year.

Vaginal sarcoma in the adult, like that in childhood, is an extremely rare entity. McFarland could collect only 58 cases. The adult sarcoma occurs in two forms, parietal and mucosal. The infiltrating parietal type is the more common.

As has been stated, the more common of the vaginal sarcomas of childhood is the botryoid type. This tumor derives its name from its chief gross characteristic, that of appearing in grapelike clusters. The anterior vaginal wall is the most common site of this lesion. It is here that McFarland found approximately 50 per cent. The posterior and left lateral vaginal walls are the next most common sites of origin. The tumor is friable, bleeds easily on manipulation, and has a tendency to become necrotic and slough. The growth is rapid, the tumor mass soon fills the entire vagina, and presents itself at the introitus as a polypoid mass of necrotic tissue. The tumor extends by continuity of tissue until, in a relatively short time, the entire pelvis is completely filled with a conglomerate mass comprising the tumor and the involved adjacent organs, i.e., vaginal vault, posterior surface of the bladder, and in its terminal stages, the rectum and the anus. The internal generative organs are involved with neoplastic tissue, which probably represents local extensions rather than lymphatic metastasis. Various authorities agree that sarcoma of the vagina in children is a mixed tumor and develops from misplaced embryonal, mesodermic cells. Microscopically, the tumor is composed of an edematous, myx-

\*Presented before the Baltimore Obstetrical and Gynecological Society, Nov. 9, 1945.

to 132½ pounds, and all urinalyses were negative. She entered the hospital on March 30, 1944, and was delivered of a normal infant weighing 5 pounds after a four-hour labor, by low forceps and right mediolateral episiotomy. Anesthesia was produced by perineal infiltration of 1 per cent procaine and pudendal block, because of a recent upper respiratory infection. The patient's postpartum course was uneventful, and she was discharged in the usual time. Nine months later, the child appeared normal in every way, and the mother's health was excellent.

### Discussion

The exact source of the liquor amnii is not known, and hence a scientific explanation for polyhydramnios cannot be given. According to DeLee,<sup>1</sup> it occurs about once in 200 cases.

From the experiments of Seechter, Carey, Carpentieri, and Darrow,<sup>2</sup> in which they demonstrated that when a watery solution was placed within the peritoneal cavity that it tended to assume the composition of a fluid in ionic and osmotic equilibrium with blood plasma, we can assume such an ionic and osmotic equilibrium for the excess accumulation of fluid within the amniotic sac.

Upon this fluid ammonium chloride acts by producing an increase in titratable acidity of the urine, producing a rise in urinary ammonia, and an increase excretion of fixed base. According to Gamble, Blackfan, and Hamilton<sup>3</sup> the diuretic action of ammonium chloride depends upon an increased acidity of the body fluids. The change in the reaction is of such a degree that it must, according to the terms of the Donnan equilibrium theory, considerably alter osmotic pressure values in the body fluids, and these alterations may reasonably be suspected as the factors involved in the removal of the body water.

We are also using ammonium chloride effectively in all stages of pregnancy, in those cases in which there is excessive gain in weight, with or without noticeable edema. In these cases, the resultant weight loss is pronounced. So far as we can determine, there has been very little use of this valuable drug during pregnancy. The results we have observed certainly suggest that this mode of treatment should receive much wider clinical trial in any condition in pregnancy in which there is undue gain in weight, or any possibility of hydramnios. A more extensive report of our experiences, along with a detailed study of the selective fluid accumulation in hydramnios and the beneficial effects of ammonium chloride, will be presented later.

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globin of 85 per cent and a red count of 4.5 million. The white blood count at this time was 5,250, with a normal differential. Routine serologic and urine examinations were negative. Cystoscopic examination showed no malignant invasion of the bladder. X-rays of the chest and pelvis showed no abnormalities.

On Sept. 21, 1939, the bulk of the growth was removed. (See Figs. 1 and 2.) Approximately one week later the remainder of the mass was excised and two 50 mg. plaques of radium were applied to the base. The radium remained in place for ten hours, giving a total dosage of 1,000 milligram hours.

Two months later a new growth had appeared on the posterior vaginal wall, with multiple small implants throughout the vault of the vagina. The growth originating on the right lateral wall appeared fibrotic and to be healed. The tumor masses were excised at this time but, because of the possibility of rectovaginal fistula, further radiation was contraindicated. Therefore, the patient was started on a course of deep x-ray therapy; a total of 2,072 "r" units was given through the four pelvic portals.

Approximately two months after the completion of x-ray therapy, the local growth showed good response, and there was no evidence of extension of the process. However, eleven months after the appearance of the first symptom, the child was readmitted for her terminal hospital stay. Symptoms reappeared approximately three weeks before this admission, consisting of anorexia, constipation, dysuria, and vaginal bleeding and discharge. Examination at this time showed marked anemia, lassitude, and moderate weight loss. The lower abdomen was distended by a mass arising from the pelvis and reaching almost to the umbilicus. Inguinal nodes were palpable for the first time. A greenish, fungating mass protruded from the vagina, associated with a profuse, foul vaginal discharge. Rectal examination confirmed the impression that the abdominal mass arose from the pelvis. On this admission there was a marked anemia and leucocytosis. The urine showed a three plus albumin and innumerable white and red cells. Supportive treatment, consisting of parenteral fluids and repeated small transfusions, was of no avail. Progress was rapidly downhill and respirations ceased at 11 A.M. on May 23, 1940, less than one year after the onset of the first symptom.

Autopsy—3340—myxosarcoma of the vagina. Necrosis and destruction of the base of the bladder. Cystitis. Hydro-ureter. Hydronephrosis. Pyelitis. Malignant infiltration of right pelvic wall. Emaciation. Dehydration. No remote metastases. (See Figs. 3 and 4.)

In contrast to the sarcoma of childhood, adult vaginal sarcoma is rarely botryoid in type, but, like the childhood tumor, the two adult forms derive their name from their predominant gross characteristic: the parietal, so named because it takes its origin from beneath the basement membrane, and the mucosal type, which involves the vaginal epithelium. The parietal type is the more common variety of adult vaginal sarcoma. The growth spreads beneath the vaginal mucosa and infiltrates the surrounding tissue. As the tumor gradually enlarges, pressure necrosis of the overlying vaginal epithelium occurs. This local extension, however, is less rapid than with sarcoma botryoides, so that the pelvic organs are not involved by the malignant process until much later. In comparison, the mucosal type, arising from a relatively small base, soon erodes through the vaginal mucosa and presents itself as a soft, necrotic tumor mass. The slough from this ulcerative, fungating mass causes symptoms to develop more rapidly, and for that reason patients with the mucosal type of tumor are usually diagnosed at an earlier clinical stage.

Microscopically, the two types of adult vaginal sarcoma cannot always be differentiated. At times the picture is classically that of a mixed tumor, while occasionally it is purely a matter of opinion. Typically, adult vaginal sarcoma

omatous stroma through which are dispersed, in varying degree, spindle and stellate cells. The nuclear activity varies from field to field; in places there will be little or no cellular activity, while other portions of the same slide will show hyperchromatic nuclei and innumerable mitotic figures. Occasionally, multinucleated giant cells are seen. Some sections will show marked vascularity, while other areas will show tissue necrosis, probably resulting from deficient blood supply. The surface of the tumor microscopically shows the characteristic changes associated with secondary infection, round cells, plasma cells, and polymorphs.

Some authorities contend that, due to its embryonal nature, botryoid sarcoma is present at birth, but is overlooked until the development of symptoms. A bloody vaginal discharge is usually the first symptom. This is frequently associated with pain and itching of the vulva and vagina. As the condition progresses, pain becomes more intense because of pressure. The pelvic mass first encroaches upon the bladder, resulting in frequency, incontinence, and infection. Quite frequently hematuria develops and indicates involvement of the bladder mucosa. With the posterior migration of the process, the rectal lumen becomes constricted; tenesmus, increasing constipation, and rectal bleeding are the natural result. Occasionally, complete intestinal obstruction ensues, with the usual signs and symptoms. Cachexia, anemia, and edema of the lower extremities appear as terminal findings. Death usually results from a combination of toxemia, uremia, and exhaustion. It will be noted from the preceding description that all symptoms are the result of local extension. Distant metastases are extremely rare, the lung and kidney being the only two sites reported in the literature.

Approximately 20 per cent of the tumors of childhood are not botryoid in type. Little is known of these miscellaneous tumors, since only ten have been reported in the literature. The gross and histologic pictures presented by these miscellaneous tumors are variable, but fundamentally resemble the adult type of vaginal sarcoma, which will be discussed later. The symptomatology of these miscellaneous tumors varies with the rapidity and extension of growth, while the prognosis is concomitant with that of the botryoid type.

CASE 1.—The first case which we wish to report represents a classical example of sarcoma botryoides. The patient is a 21-month-old, white, female child, admitted Sept. 19, 1939, to the gynecologic service at the University of Maryland. The chief complaint on admission was vaginal bleeding of three months' duration. The patient developed normally until, at the age of 18 months, the mother first noticed small clots of blood passing from the vagina. The child exhibited no other symptoms or signs, and medical attention was not sought for approximately two months. On the advice of the family physician the child was hospitalized at the Washington County Hospital, at Hagerstown, Maryland. Several small tumors were removed from the vagina which histologically proved to be sarcomatous. The postoperative course was uneventful, but vaginal bleeding occurred in three weeks. It was then that the patient was first referred to the University of Maryland Hospital for further study and treatment, since the facilities for radiation therapy were lacking at Hagerstown. The remainder of the history was entirely negative and indicated no familial tendency toward malignancy. General physical examination at the time of admission was essentially negative, and there was no evidence of weight loss or anemia. Examination of the pelvis showed the vulva to be normal. Protruding from the vaginal outlet was a small, polypoid mass apparently arising from the right lateral wall, near the right fornix. The remainder of the pelvic organs, as far as could be determined, were not involved at this time. Laboratory examination shortly after admission showed a hemo-

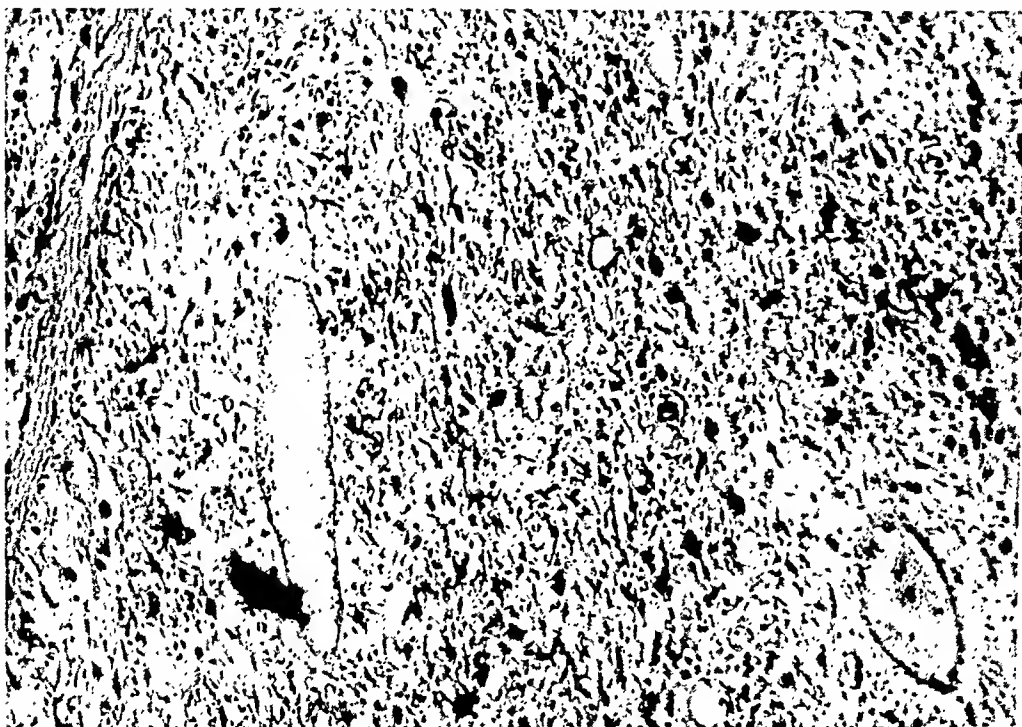


Fig. 3.—Sarcoma botryoides after therapy, autopsy section (low power).

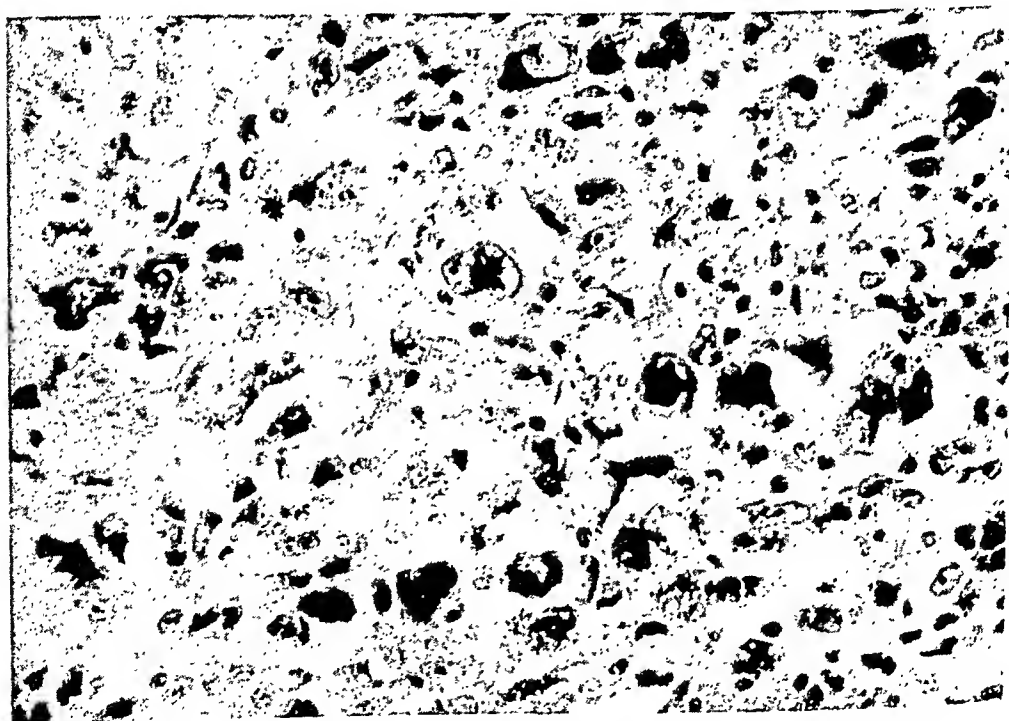


Fig. 4.—Sarcoma botryoides after therapy, autopsy section (high power).

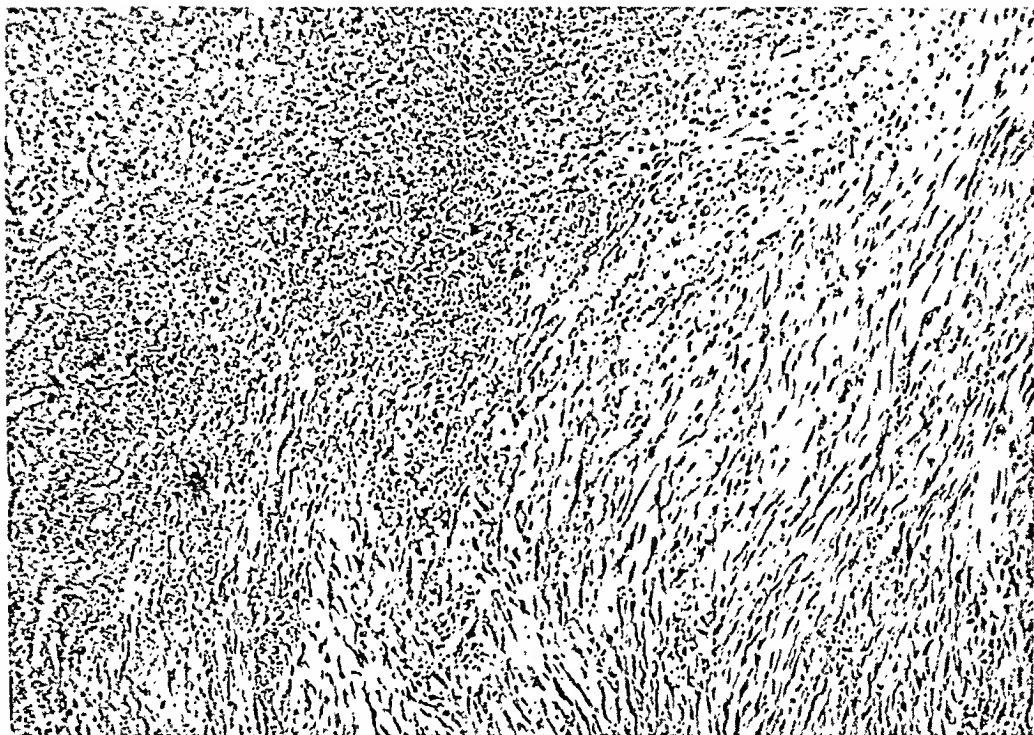


Fig. 1.—Sarcoma botryoides before therapy (low power).

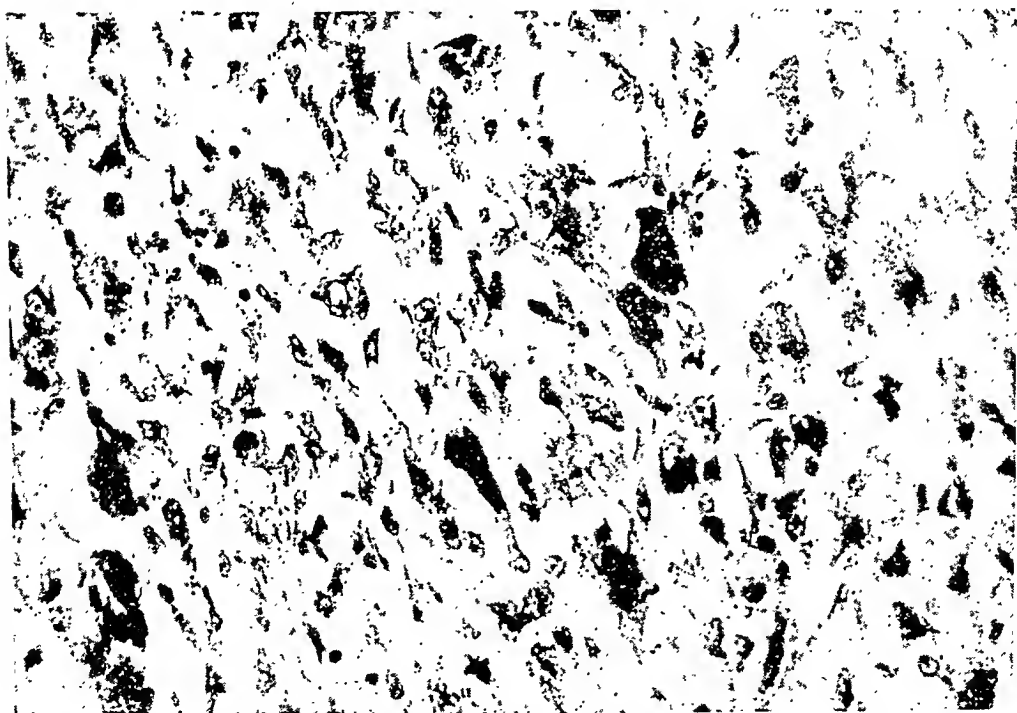


Fig. 2.—Sarcoma botryoides before therapy (high power).





Fig. 5.—Fibrosarcoma before therapy (low power).

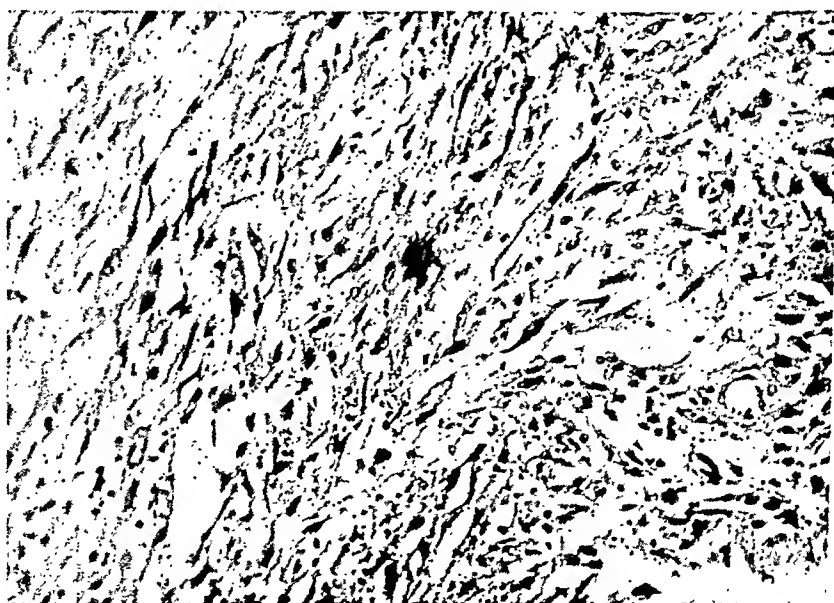


Fig. 6.—Fibrosarcoma before therapy (high power).

consists of bundles of spindle cells dispersed through a highly vascular stroma. The cells are quite uniform in size and shape; mitotic figures and hyperchromatic nuclei are moderately numerous. Tumor necrosis is usually present with the associated appearance of secondary inflammatory cells.

From the gross description of the lesions, it is obvious that the symptoms, while similar, will occur earlier with the mucosal variety. Chronologically, they appear as a vaginal discharge which soon becomes malodorous. As ulceration takes place, bleeding occurs, usually first noted and more profuse following trauma. As the infiltration of the vesicovaginal and rectovaginal septa progresses, the classical bowel and bladder symptoms ensue. The subsequent sequence of events, though less rapid, is identical with that of sarcoma in children, and ultimately terminates in toxemia and death. Symptoms resulting from distant metastases are somewhat more common than those found in the childhood type. Lung, kidney, omentum, liver, and long bones have all been reported as a site of metastatic lesions.

CASE 2.—The presentation of a typical recent case of adult vaginal sarcoma follows: this patient, a 40-year-old Negro woman, was admitted to the gynecologic service July 23, 1945, with a chief complaint of a "sore" in the vagina and lower abdominal pain of eight weeks' duration. The patient was apparently well until two months prior to admission, when she first noted a tender, hard area within the vagina. There was some vaginal discharge and slight bleeding on trauma. There were no other subjective symptoms, excepting moderate discomfort in the lower abdomen, suggestive of recurrent chronic salpingitis. Both the family and past history were entirely negative. The patient had had no serious illnesses or operations. The review of systems was negative, as was the menstrual history. The patient was married but had had no pregnancies, although there was a vague history of a spontaneous abortion in March, 1945.

General physical examination revealed a moderately obese Negro woman, without evidence of anemia or weight loss. Examination of breasts and abdomen was entirely negative. There were no palpable inguinal nodes. Pelvic examination revealed the external genitals normal and the outlet marital, with good support. On the right anterolateral vaginal wall, about mid-distance between the introitus and cervical portio, was found a walnut-sized, round, granular lesion. The growth measured  $3\frac{1}{4}$  cm. in greatest diameter, and the exposed surface was covered with a grayish white exudate. Induration was present in the submucosal tissue surrounding the elevated portion of the lesion. This was more marked anteriorly, where it extended almost to the base of the urethra. The cervix was small, firm, entirely separate from the vaginal growth, and there was no erosion or malignancy on inspection. The uterus, tubes, and ovaries were normal. Rectal examination showed no evidence of parametrial extension.

Laboratory investigation of the blood, made during hospitalization, indicated that all cytologic and chemical constituents were within normal limits. Liver and renal function tests showed no evidence of impairment. Complete x-ray studies revealed no osseous metastases. Cytoscopy showed no evidence of extension.

On the seventh day after admission, the following operative procedure was carried out on the previously described lesion. A portion of the growth was removed in such a manner that a flat surface remained. (See Figs. 5 and 6.) Against this was placed a plaque containing 100 mg. of radium, with a 3 mm. lead equivalent filter; this plaque was held in position with one vaginal pack and remained in place for thirty hours, giving a total dosage of 3,000 milligram hours. The postoperative course was entirely uneventful and the patient was discharged to the Oncology Clinic after a hospital stay of seventeen



Complete surgical excision is usually impossible and, while the tumor is radiosensitive, recurrences rapidly develop.

The prognosis is uniformly poor, and the diagnosis is open to question in any case which survives more than two years.

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days. Since discharge from the hospital, the patient has returned frequently for follow-up examinations. At these times it has been noted that there is a gradual local regression of the growth, and no evidence of further extension.

### Comment

The treatment of sarcoma of the vagina is most discouraging. Because of its extremely malignant nature and rapid growth, the tumor is soon beyond the realm of favorable response to surgery or/and radiation. Since all types of vaginal sarcoma consist of the same histologic elements, the treatment is fundamentally the same, but, because of the rarity of this condition, no uniformity of treatment has been established, and each case presents a problem in therapeutics. Surgery, electrosurgery, and radiation are the means available for the treatment of these malignant tumors, and usually are combined in the management of any specific case. Excision is most certainly indicated in the botryoid tumor where the entire vagina is filled with grapelike clusters. This procedure at times is difficult because space is limited and exposure inadequate. The pedicle is extremely vascular, and hemorrhage is always a potential danger. In spite of these apparent contraindications, the procedure must be undertaken in order to make the base accessible for radiation therapy. Electrosurgery is often the procedure of choice, especially when ligation of individual bleeding points is impossible. The total extirpation by either surgery or electrosurgery is usually impossible, due to the inaccessibility of the growth, occasioned by its rapid migration. The excision of local recurrences is indicated, particularly in the presence of ulceration, bleeding, and secondary infection.

Since sarcomas in general are radiosensitive, vaginal sarcomas theoretically should respond if all the cells could be brought within the effective sphere of the ray. As has been previously described, the base of the tumor must be adequately exposed in order that it may be amenable to the application of a radium plaque. The plaque usually consists of 100 mg. of radium, and is made to conform to the size and shape of the lesion. The plaque itself is so constructed that the rays from each of the five separate cylinders are directed against the growth. The surrounding structures are protected by a lead shield, and the irritating rays are eliminated by a 3 mm. lead equivalent filter. A large vaginal pack is used to maintain the plaque in its original position, and at the same time it distends the vagina and further protects the bladder and rectum from the radium rays. In order to avoid the possibility of stricture, the radium is employed in two or three divided doses, each of them from 1,000 to 3,000 milligram hours.

Roentgen therapy is often used as an adjunct to surgery and radium, and in these cases the total dosage of deep x-ray depends upon the local response. The x-ray is given in divided doses through the usual pelvic portals.

The time interval between the three different types of therapy must be based upon the therapeutic response to each phase of treatment.

Local recurrences of the growth should in general be handled in the same manner as the original lesion.

### Summary and Conclusions

Sarcoma of the vagina, like sarcoma in general, is a highly malignant tumor of mesoblastic origin. It is classified in two main types, childhood and adult. The botryoid is the more common childhood form, while the parietal is the more common adult variety.

The progress of the disease is rapid, and the signs and symptoms are the result of local extension.

*Second Pregnancy.*—Uneventful. Blood pressure range 112/72 to 135/85; no proteinuria or edema; total weight gain was 14 pounds. Delivered Dec. 21, 1933, of a living child at forty-two weeks. The placenta was adherent to the site of the previous molar implantation, and was removed manually four hours after delivery. The blood loss was estimated at 900 ml., and the patient went into shock which was successfully treated. Febrile morbidity occurred for the first seven days, and then a normal puerperium.

*Third Pregnancy.*—Uneventful. Blood pressure range 110/60 to 120/76; no proteinuria, slight pretibial edema when near term, total weight gain again 14 pounds. Delivered March 25, 1936, of a living child at forty-one weeks. Normal puerperium occurred.

*Fourth Pregnancy.*—Central placenta previa and cesarean section at thirty-four weeks, Sept. 8, 1937. Blood pressure range 86/62 to 125/65. No proteinuria; no edema; total weight gain, five pounds. Baby survived, and the mother's convalescence was smooth.

*Follow-up, Nonpregnant.*—In April, 1940, her blood pressure was 122/76; urea clearance was normal; heart was not enlarged; eyegrounds were normal.

*Fifth Pregnancy.*—Patient came into the clinic Aug. 19, 1940, with an amenorrhea of fourteen weeks, and complaining of a brownish vaginal discharge, nausea and vomiting of six weeks' duration, and a weight loss of 18 pounds. The uterus was unusually soft, the size of a four and one-half months' pregnancy. No fetal heart, movement, or parts could be made out. Friedman tests were positive in urine dilutions as high as 1 to 9,000, and in spinal fluid diluted 1 to 200. The blood pressure was normal, and there was no proteinuria or edema; red blood count was 3,900,000, and basal metabolic rate, plus 44 per cent.

In the second week of hospitalization, the patient gained 5 pounds; edema appeared; the blood pressure mounted to 170/110, and later to 206/140. Proteinuria appeared and rapidly increased to as much as 30 Gm. per liter. The blood uric acid rose steadily from 4.2, and ultimately reached 8.5 mg. per 100 ml. On the nineteenth hospital day, she had five eclamptic convulsions. When these had been controlled, a bag was inserted to induce labor, and about fifty hours later a large hydatidiform mole was expelled. Remnants of the mole were removed digitally. Blood culture taken at the time of an intrapartum chill showed anaerobic streptococci. In the first four days of the puerperium, the patient ran a septic course, and received multiple small transfusions. Thereafter, the convalescence was smooth. The Friedman test was positive in half strength on the eighth day, in full strength on the fifteenth day, and negative on the twenty-second day.

Five weeks after the delivery of the mole, the patient began to have intermittent pain in the left lower quadrant, at first with slight vaginal bleeding and passage of clots, and then with profuse hemorrhage. She was readmitted in mild shock. An exquisitely tender mass (cystic ovary on a twisted pedicle) was palpated at the site of the pain. After anti-shock therapy, a diagnostic curettage was done. The pathologic report was "atypical chorionepithelioma." After further transfusions, complete hysterectomy and bilateral salpingo-oophorectomy were done. The uterus was twice the normal size; the left ovary was replaced by a cyst weighing 180 Gm.; the right ovary was smooth, cystic, and completely degenerated. The uterus showed a single nodule of chorionepithelioma. Recovery was uneventful.

At follow-up ten months later, the patient was in good health. The blood pressure was 118/70; no proteinuria was present; the urea clearance was 86 per cent. She, together with her entire family, was killed in an automobile accident the day after leaving the hospital.

## HYDATIDIFORM MOLE, WITH SPECIAL REFERENCE TO RECURRENCE AND ASSOCIATED ECLAMPSIA

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WE HAVE encountered in our clinic an unusual case of recurrent hydatidiform mole complicated each time by severe toxemia, which has stimulated us to analyze all of our "mole" cases and to review certain aspects of the literature. In the present paper, we shall give:

1. A case report—hydatidiform mole with severe pre-eclampsia, followed by three normal pregnancies, and then another mole with eclampsia and a subsequent chorionepithelioma, despite negative Friedman tests.
2. A review of the literature on recurrent hydatidiform mole.
3. A review of the literature on eclampsia associated with hydatidiform mole.
4. An analysis of 57 consecutive cases of hydatidiform mole, with follow-up studies on all.

### Case Report

*First Pregnancy.*—B. B., history No. 3409, aged 22 years, gravida i, para 0, came into the clinic on Feb. 23, 1932, in the third month of pregnancy. She complained of marked edema of the extremities of two weeks' duration. She had dyspnea on slight exertion, hemoptysis, and vaginal spotting. Her weight was 117 pounds; blood pressure, 180/130; 4 plus proteinuria; with marked edema to the hips and of the arms. The abdomen was flat, and the fundus was 11 cm. above the symphysis. She was admitted to the hospital at once, and during the next six weeks maintained the hypertension and proteinuria. The edema became generalized and then cleared up under dehydration therapy, with a weight loss of 18 pounds. A transfusion was given because of anemia (red cell count of 3,060,000). On x-ray examination, the heart appeared to be generally enlarged. The optic fundi showed white patches and silvery arteries. The urinary specific gravity varied from 1.003 to 1.016; numerous hyalin and finely granular casts were a constant finding. The two-hour excretion of phenol-sulfonphthalein was 40 per cent, with none appearing by the end of the first thirty minutes. The blood nonprotein nitrogen and uric acid were normal at all times. After six weeks in the hospital, she spontaneously expelled a hydatidiform mole, following which the uterus was digitally everted.

After expulsion of the mole, the blood pressure dropped, although it remained at 140/90 to 100 for several weeks before falling to normal levels. The proteinuria cleared up rapidly, but reappeared sporadically during the next three months. The uterus involuted slowly, and was still slightly enlarged three and one-half months later. The left ovary, which had been enlarged, regressed with equal slowness.

The Friedman test was negative two weeks after extrusion of the mole, but became positive three months later. Because of two positive tests, in the absence of probability of pregnancy, a diagnostic curettage was done. The pathologist's report on the curettings was "chronic endometritis." Recovery was smooth.

Nine women having *three* moles are recorded by Steinberger,<sup>34</sup> Haase,<sup>16</sup> Depaul,<sup>8</sup> Warman,<sup>37</sup> Buzzoni,<sup>6</sup> Haas,<sup>15</sup> Morosi,<sup>27</sup> Thomas,<sup>36</sup> and Jeffreys and Graffagnino.<sup>19</sup>

Three case reports have been published describing *four* moles in the same patient: Osborn,<sup>30</sup> Fritsch,<sup>13</sup> and Digonnet.<sup>10</sup>

Lemaire<sup>22</sup> described a case having *six* moles, Muggia<sup>28</sup> one with *seven* (third complicated by eclampsia), Maek and Catherwood<sup>24</sup> one with *ten*, and Essen-Möller one with *eighteen* moles. (These cases with the higher numbers are based upon the histories elicited from the patients.) Krieger<sup>21</sup> reported a case in which *three* consecutive pregnancies terminated in stillbirths accompanied by progressively decreasing degrees of partial molar degeneration.

In the cases cited above, the hydatidiform moles occurred in successive pregnancies, or were separated by early abortions. The interspersing of normal pregnancies between moles seems to be unusual. Harkin<sup>17</sup> described a case in which the first and third pregnancies were molar, while the second went normally to term. Kohn's<sup>20</sup> case had two normal pregnancies, a mole, then eight normal pregnancies, and finally a fatal mole. Rosenthal<sup>33</sup> reported a case having 11 normal pregnancies, a mole, two normal pregnancies, and again a mole. Bazán<sup>1</sup> reports a case in which the first three pregnancies were normal, the fourth and fifth molar, the sixth and seventh normal, and the eighth again molar. Bottiroli's<sup>4</sup> case is very similar: four normal pregnancies, fifth and sixth molar, seventh normal, and eighth again molar.

There are three cases cited which we have been unable to see. Lemaire<sup>22</sup> credits to Virchow a patient having two moles. Essen-Möller<sup>11</sup> refers to Hermont as having a patient with six consecutive moles. Madame Boivin<sup>3</sup> refers to a case of Bonus in whom three consecutive moles may have occurred within a period of a few months.

We are eliminating a group of possible cases, for the reasons given in each instance. Findley<sup>12</sup> referred to a case of Lönberg and Mannheim<sup>23</sup> as having a mole followed by a normal pregnancy and then another mole. (We believe that we have found the case. Findley's reference is to "Lönberg and Mannsheimer," and the place of publication given was erroneous.) The patient did have a mole in her first pregnancy, and the second pregnancy was normal. Chorionepithelioma was found four weeks after the normal pregnancy. The writers suggested the possibility of an unrecognized mole associated with the chorionepithelioma. Since they, who managed the case, did not recognize a recurrent mole, we shall not. Both Essen-Möller<sup>11</sup> and Lemaire<sup>22</sup> (both of whose reviews of the literature have been extensively transcribed, translated, and transmuted by many later writers) wrote that Mayer had a case with 11 consecutive premature deliveries. Each baby was well formed, and accompanied by a mole. Majer<sup>25</sup> (variously called Maier, Meier, Major, Mayer and Meyer in different citations) did describe such a case, but writes "... und die sich als gewöhnliche, 12 Loth schwere Fleischmole darstellte." It is not stated that the Fleischmolen, only the last of which Majer saw, had undergone hydatidiform degeneration. Our inclination is to throw out this case, which has been cited in literally dozens of secondhand reviews of the literature. Lemaire<sup>22</sup> cites O. Ashby as having a case with three moles in three years; Essen-Möller<sup>11</sup> says that Osborn Ashley described three moles in three years. These two citations almost certainly should be to G. Ashby Osborn,<sup>29</sup> who described such a case in 1864, and in 1865 reported the fourth mole in the same patient.<sup>30</sup> Lemaire<sup>22</sup> writes, "Haase, Warman et Bloek, Krieger, Virchow et Williamson" described cases having two moles (how many case reports here? two? six? any intermediate number?). Compare these names with some of those cited above. While "Haase, Warman et Bloek" looks like a single paper by three authors, Bloch<sup>2</sup>

In recapitulation, the patient had a hydatidiform mole in her first pregnancy. This mole was accompanied by severe pre-eclampsia. Three months later, the Friedman test became repeatedly positive, after having been negative. No reason was ever found for this. She then had three pregnancies without mole and without toxemia. Two of these were characterized by anomalous placentation. The fifth pregnancy was again molar, and with this mole she had eclampsia. Five weeks after the mole was expelled she developed signs of chorionepithelioma, which diagnosis was confirmed. The Friedman test was negative at three weeks, and only weakly positive at five weeks, despite the presence of the neoplasm. Cystic ovaries occurred with both of the moles. The patient was followed in all of her pregnancies, between pregnancies, and until her accidental death.

### Review of the Literature

*Recurrence of Hydatidiform Mole.*—There seems to be no estimate in the literature as to the frequency of recurrence of mole. Several series of 50 to 100 or more cases have been published, with no instance of recurrence in these consecutive cases. Mathieu<sup>26</sup> analyzed a series of 127 cases pooled by the Pacific Coast Obstetrical and Gynecological Society over a five-year period. One of these patients gave a history of having had an earlier mole. There were 16 patients having subsequent pregnancies, and one of these had simultaneously another mole and chorionepithelioma. It is not clear whether one patient is involved twice in this account, or whether there were two patients having repeated moles. Holman<sup>18</sup> surveyed the cases of the following five years. By coincidence, there were again 127 patients, of whom one gave a history of an earlier mole. Brews<sup>5</sup> reviewed the 100 cases of hydatidiform mole occurring in a 33-year period at the London Hospital. Only one of these gave a history of previous mole, and none had a subsequent mole. Jeffreys and Graffagnino,<sup>19</sup> in a series of 28 cases, saw one patient who had two moles, and one who had three. In the 13-year experience of the Margaret Hague Maternity Hospital, there have been 57 cases of mole, with only one recurrence (case report). None of the 56 patients gave a history of having had an earlier mole elsewhere.

Essen-Möller,<sup>11</sup> in 1912, reviewed the literature and found 10 case reports of recurrent mole, to which he added two cases of his own. Since there seems to be no more extensive review than his, we have made a rather thorough search for case reports of repeated mole. Our procedure was to look through the *Index Medicus* from 1879 to date, the *Index Catalogue of the Surgeon General's Library* from 1880 to date, and the *Berichte über die gesamte Gynäkologie und Geburtshilfe* from 1924 to date. Also, we looked through the general indices of many journals, especially the German. We then gained access to the papers with titles suggesting that the subject matter might be concerned with molar pregnancy in relation to (a) recurrence, (b) toxemia, and (c) analyses of large series of cases. Also, we have consulted publications cited in the bibliographies of papers germane to our subject, whenever they could be found.

We shall first cite chronologically the papers which we have actually seen; to these may be added three which were not found. Still other references will be discussed and rejected.

Seventeen (or 18) women having *two* moles have been reported by van Deurs,<sup>9</sup> Bloch,<sup>2</sup> Puech<sup>32</sup> (two cases), von Winekel<sup>39</sup> (not four moles as stated by Essen-Möller—the author writes that the first and third pregnancies terminated as blood moles, while the second and fourth were hydatidiform moles), Williamson,<sup>38</sup> Findley,<sup>12</sup> Essen-Möller,<sup>11</sup> Muggia,<sup>28</sup> Cipriani<sup>7</sup> (doubtful case), Guiryo,<sup>14</sup> Paseale<sup>31</sup> (first mole complicated by eclampsia), Mathieu<sup>26</sup> (one or two cases?), Brews,<sup>5</sup>ureau,<sup>35</sup> Holman,<sup>18</sup> and Jeffreys and Graffagnino.<sup>19</sup>

TABLE I. CASES OF PROBABLE OR ALLEGED ECLAMPSIA OCCURRING IN CONJUNCTION WITH HYDATIDIFORM MOLE

AUTHOR	YEAR	LOCALITY	MONTHS PREG- NANT	FETUS	AGE	PARITY	PREVIOUS ABORTION
Malichecq <sup>62</sup>	1866	Mont-de-Marsan	4 to 5	0	24	Multip.	0
Meye <sup>63</sup>	1869	Halle	4	Yes	34	Primip.	Yes
Parmenter <sup>65</sup>	1870	Michigan	?	0	53	Multip.	?
Almy <sup>41</sup>	1882	Connecticut	4	0	?	?	?
Dulac <sup>47</sup>	1884	Paris	5	0	37	Primip.	0
Chadwick <sup>44</sup>	1890	Boston	4	0	25	Primip.	0
Falk <sup>48</sup>	1897	Jena	5	Yes	22	Primip.	0
Raineri <sup>66</sup>	1904	Vercelli	3	?	?	Multip.	?
Hitschmann <sup>56</sup>	1904	Vienna	5	0	18	Multip.	0
Rossi-Doria <sup>67</sup>	1906	Rome	4	?	30	Multip.	?
Rossi-Doria <sup>67</sup>	1906	Rome	3 to 4	?	21	Primip.	0
Kroemer <sup>60</sup>	1907	?	4 to 5	?	30	Multip.	?
Dienst <sup>46</sup>	1908	Breslau	4 to 5	Yes	32	?	?
Gross <sup>51</sup>	1909	Prague	5	Yes	22	Multip.	0
Brauser <sup>42</sup>	1910	Munich	5	0	34	Multip.	0
Sitzenfrey <sup>70</sup>	1911	Giessen	6	0	22	Primip.	0
Vineberg <sup>72</sup>	1911	New York	6	0	25	Primip.	0
Vineberg <sup>72</sup>	1911	New York	4	0	18	Primip.	1 (?)
Jonas <sup>58</sup>	1914	Greifswald	7	Yes	?	?	?
Albeck <sup>40</sup>	1914	Denmark	?	?	30	Multip.	?
Westermark <sup>73</sup>	1919	Stockholm	6	0	25	Multip.	0
Muggia <sup>28</sup>	1920	Milan	3	?	23	Primip.	2 moles
Guggisberg <sup>52</sup>	1922	Berne	4	0	?	Primip.	0
Hinselmann and Nettekoven <sup>55</sup>	1922	Bonn	6	0	42	Multip.	0
Hinselmann and Nettekoven <sup>55</sup>	1922	Bonn	4	?	?	?	?
Herring <sup>53</sup>	1924	Pingtu	4 to 5	Yes	35	Multip.	0
Lahm <sup>61</sup>	1924	Dresden	3	Yes	?	?	?
Frey <sup>49</sup>	1924	Aarau	5 to 6	0	29	Primip.	0
Sarry and Bogdan <sup>68</sup>	1925	Roumania	3	0	27	Multip.	0
Brouha <sup>43</sup>	1927	Liège	5	0	49	Multip.	?
Wigger <sup>74</sup>	1928	Königsberg	5	?	29	Multip.	0
García <sup>50</sup>	1929	Chile	?	0	?	Multip.	0
Pascale <sup>31</sup>	1934	Benevento	4	0	34	Multip.	0
Jiménez <sup>57</sup>	1935	Spain	4	0	27	?	?
de Snoo <sup>71</sup>	1937	Rotterdam	?	?	16	Primip.	0
Own case	1946	Jersey City	4 to 5	0	30	Multip.	1 mole

### Analysis of 57 Cases of Hydatidiform Mole

From the opening of The Margaret Hague Maternity Hospital, Oct. 16, 1931, until Dec. 31, 1944, there have been 75,238 deliveries and 57 cases of hydatidiform mole. This gives an incidence of 0.07 per cent, or one in 1,321. The usual incidence is considered to be somewhat lower—about 1 to 2,000. Our incidence in private patients was 1.7 times that in the ward cases. The distribution by age and parity roughly paralleled the distribution of deliveries by age and parity. Five of the moles occurred in primigravidas of less than 20 years of age, and 25 were seen in primigravidas older than 20 years. Of the 27 multigravidas, 26 per cent had had previous abortions (none of these knew of having had an earlier mole).

In 12 cases (21 per cent) the diagnosis of hydatidiform mole was suggested before the extrusion or removal of vesicles. Cystic ovaries were diagnosed in four cases. A fetus was present in four cases: two of these were twin preg-

did describe a case with two moles. Haase,<sup>16</sup> Haas,<sup>15</sup> and Warman<sup>37</sup> have each reported cases with three (not two) moles. Essen-Möller<sup>11</sup> attributes to "Hasse" a case having two moles, and Bazán<sup>1</sup> credits "Hause" with such a case. The misspelling of a name by one letter is a mere peccadillo as the bibliographies of these case reports go. Since we have cited the cases of Krieger,<sup>21</sup> and of Williamson,<sup>38</sup> as well as the three just mentioned, we believe that the only case from this welter which we do not have is that of Virchow. Muggia<sup>28</sup> mentions a case of "Karkin" (reference merely to "Da Naccioli") which fits in all details with the case of Harkin.<sup>17</sup>

In summary, then, we have found descriptions of 39 or 40 women having recurrent moles. In addition to these, we have seen citations to two cases, and possibly more. Of these 41 or 42 women, only five had normal pregnancies between moles. To this list, we add our own patient who had a mole in her first pregnancy, then three normal pregnancies followed by a recurrent mole in her fifth pregnancy.

*Eclampsia in Molar Pregnancy.*—We have found in the literature 35 cases of probable or alleged eclampsia occurring in association with hydatidiform mole, or with partial hydatidiform degeneration of the placenta. These are summarized in Table I. There are more papers than cases; thus one of the cases described by Hinselmann and Nettekoven<sup>55</sup> was earlier reported both by Schäfer<sup>60</sup> and by Knopp.<sup>59</sup> The case often credited to Olshausen<sup>64</sup> was described 22 years previously by Meye.<sup>63</sup> Chadwick's<sup>44</sup> case was later mentioned by Craigin,<sup>45</sup> to whom it was credited by Essen-Möller.<sup>11</sup> Another duplication is in the case described by Falk<sup>48</sup> and by Hillman.<sup>54</sup>

Hinselmann and Nettekoven<sup>55</sup> mention cases of Döderlein and Rosinski, but give no reference to the original reports. We have not found these, but from Hinselmann's remarks, Döderlein's case seems to check in all details with the case described by Brauser,<sup>42</sup> from Döderlein's clinic. We have no lead at all to Rosinski's case, unless it is the remarkable one in which eclampsia occurred with a missed abortion (no hydatidiform degeneration here, however).<sup>75</sup>

Westermarck's<sup>73</sup> case, described as eclampsia, is open to serious question, since the patient had no proteinuria and the convulsions did not occur until eight and one-half weeks after the evacuation of the uterus. Raineri's<sup>66</sup> case had convulsions and died ten days after a spontaneous abortion, but he found molar tissue post mortem, which would make this case acceptable. Dulac's<sup>47</sup> patient had convulsions two and one-half weeks after the passage of a mole; however, she had continued to pass vesicles for a few days afterward, and had an offensive vaginal discharge until the day of convulsion. Dienst's<sup>46</sup> patient had no actual convulsion, but was comatose for three days, and had twitchings and marked proteinuria. Dienst's diagnosis was, regretfully, "Eklampsie ohne Anfall." García's<sup>50</sup> case had no convulsion, but postmortem examination established the presence of eclamptic changes in the liver and kidneys.

Only partial molar degeneration was present in the cases of Meye,<sup>63</sup> Falk,<sup>48</sup> Dienst,<sup>46</sup> Gross,<sup>51</sup> Jonas,<sup>58</sup> and Wigger.<sup>74</sup> In 19 cases in Table I, the definite statement is made that no fetus was present. A fetus was said to occur in seven, and in 10 no explicit statement is made, but one gets the impression that there was no fetus.

Five of the 36 cases died, a mortality of 14 per cent. This seems low when one considers the mortality rate for mole alone, or for eclampsia alone during the times when most of these cases occurred.

The ratio of primiparas to multiparas is 2 to 3. This is distinctly at variance with the ratio noted in any considerable series of eclamptics, where primiparas outnumber multiparas almost to 3 to 1.



2. Persistence of positive Friedman test. After delivery of the mole, the Friedman test, in about half of the series, became negative as follows: five in the first week, four in the second week, nine in the third week (one of these developed chorionepithelioma—case report), five in the fourth week, three in the fifth week, and three between the sixth and ninth weeks.

Of the tests remaining positive post partum, two occurred in patients with chorionepithelioma. The test was persistently positive for months in two other cases. One of these went to a private physician after two months, and we did not see her again for twelve years. In the other case, the Friedman test was positive in urine diluted 1 to 50 as late as four months post partum; at five months it was weakly positive in undiluted urine, and became negative seven and one-half months after the mole had been removed at hysterotomy. Hamburger,<sup>78</sup> in a follow-up study of 72 cases of hydatidiform mole, found that 9 per cent were still excreting gonadotropin three months after evacuation of the uterus. All tests were negative at six months post partum.

*Chorionepithelioma.*—Three patients had chorionepithelioma. These are the only cases which have been seen in our service, and all followed hydatidiform mole. All were hysterectomized and all survived. One of the three had a misleading Friedman test (case report). This patient died accidentally about ten months after hysterectomy. The other two patients are alive and well at nine and one-half and eleven years after operation.

### Follow-Up

Every patient was followed up for at least one year, and the average length of follow-up is over six years. Three patients have died. One death was accidental (case report), one of myocardial failure seven and one-half years post partum, and the third was an eclamptic death, occurring in the next pregnancy (in another hospital), two and one-half years after the mole. Of the 53 surviving women, all but two have been interviewed during 1945.

The only untoward postmolar incident occurred in a private patient who did not return to her physician after discharge from the hospital. About five months after discharge, she had a severe hemorrhage and passed a hydatidiform mole the size of a football. She was curetted in another hospital, and referred to Dr. Sehumann, in Philadelphia. At hysterotomy, he found no molar remnants. In our hands, she had had a second curettage when bleeding persisted after the initial operation. At follow-up, seven years later, she stated that she had had a normal menstrual period after leaving the hospital. Possibly she had a second molar pregnancy.

*Subsequent Pregnancies.*—Thirty-nine of the patients have had 66 (or 67?) pregnancies subsequent to their moles. One patient had a second mole (case report), and another, just alluded to, may have had. There was one tubal pregnancy, and there were six spontaneous abortions. In the case of the fatal eclampsia, mentioned above, the baby was stillborn. Thus, in 66 pregnancies 57, or 87 per cent, eventuated in live births.

Of the nine cases with mole and toxemia, two did not become pregnant again. There were 13 later pregnancies in the other seven. Three of these seven had four toxemias, one of which was fatal eclampsia, and another a severe eclampsia (case report).

*Menstrual Data.*—Two patients were hysterectomized at the time of the mole, and three others shortly thereafter, because of chorionepithelioma. Later hysterectomy was done for fibroids in two more patients.

We could find no characteristic disturbances in the menstrual histories, either before or after the molar pregnancies. In one patient, a previously normal cycle was completely suppressed for three years following the mole, but spon-

nancies, and the other two were true abortions with molar degeneration of the placenta. There were no maternal deaths.

*Signs and Symptoms.*—1. Bleeding occurred in 96.6 per cent—all but two cases.

2. Secondary anemia, as manifested by red blood cell counts of less than 4,000,000, was observed in 19 patients. Blood transfusions were given in 14 cases.

3. The uterus was larger than to be expected from the period of amenorrhea in 33.3 per cent of cases. It was almost as frequently too small, and sometimes of the expected size.

4. Pre-eclampsia occurred in eight cases, and eclampsia in one, giving a toxemia incidence of 15.8 per cent. By pre-eclampsia, we mean blood pressure greater than 140/90 and proteinuria. Marked proteinuria (3 and 4 plus) occurred in another three patients whose blood pressures were less than 140/90.

5. Weight loss was noted in six cases. It probably occurred in others, but only a few charts carried any notation of the weight changes.

6. Friedman tests were done before evacuation of the uterus in only 11 instances. All were positive. Of these, three were done only with the usual quantity of undiluted urine. The other eight were done in dilution, and all were positive with less than 0.1 ml. of urine. The highest dilution giving a positive reaction was 1 to 9,000, while the same urine diluted 1 to 10,000 was negative. Usually the liminal concentration of gonadotropic hormone was not determined.

*Toxemia in Molar Pregnancy.*—The association of pre-eclampsia with hydatidiform mole is so frequent and so well known that Hitschmann,<sup>76</sup> in his monograph on mole, included early pre-eclampsia as one of the diagnostic criteria. The incidence of toxemia has been variously set at from less than 10 to more than 40 per cent. Hitschmann's review indicates about 30 per cent as a fair average.

Page<sup>77</sup> divided his cases into two groups, which he called "early stage" and "late stage." In 16 patients of less than four months' amenorrhea, or with the tumor below the level of the umbilicus, none had toxemia. In 14 patients with more than four months' amenorrhea, or with the tumor above the level of the umbilicus, 10, or 71 per cent, had toxemia. In our series, 25 patients are classifiable as "early stage"; none of these had toxemia, although two had proteinuria without hypertension. In the 32 patients in the "late stage," there occurred nine cases of toxemia and 1 case of proteinuria without hypertension.

As for the degree of toxemia, eclampsia occurred in one patient; the same patient had severe pre-eclampsia with her first mole (case report). The other seven toxemias were classifiable as "mild pre-eclampsia" by the criteria of the American Committee on Maternal Welfare (ignoring the time of onset).

*Labor and Delivery.*—Labor was of spontaneous onset in 33 patients (58 per cent); it was induced by bag or bougie in five, and there was no labor in 19 (33 per cent). Delivery of the mole was spontaneous in 34 cases (60 per cent), 21 of whom had a curettage after extrusion of the mole. In 13, the mole was removed by curettage alone. Four moles were removed manually, four by abdominal hysterotomy, one by abdominal hysterectomy, and one by sponge stick.

*Puerperium.*—1. Febrile morbidity. Six cases, or 10½ per cent, had febrile morbidity. Of the 19 patients having no labor, none was morbid. Five of the 33 having spontaneous labor were morbid, as was one of the cases induced by bag (case report). All six of the febrile patients were delivered spontaneously, four of them having had a subsequent curettage.

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taneously reverted to normal at the end of that time. Only one patient gave a history of menstrual irregularity, and that antedated the mole. Seven patients think that their periods are shorter or scantier than before the mole, and six think the reverse. All of the rest have noted no deviation from normal, and no change since their moles.

### Summary

A case is reported in which the first pregnancy gave rise to a hydatidiform mole accompanied by severe toxemia. This was followed by three normal pregnancies with no sign of toxemia, although anomalous placentation occurred in two. The fifth pregnancy was again a hydatidiform mole, accompanied by eclampsia, and followed by chorionepithelioma. The Friedman tests were misleading in this case.

A review of the literature had revealed descriptions of about 40 cases of recurrent hydatidiform mole. Only five of these women had normal pregnancies occurring between moles.

We have found 35 cases of probable or alleged eclampsia in conjunction with hydatidiform mole.

In over 75,000 deliveries at The Margaret Hague Maternity Hospital, there have been 57 cases of hydatidiform mole (through 1944), giving an incidence of 1 to 1,321.

Three of these moles were followed by chorionepithelioma.

There were no maternal deaths.

The 57 cases of hydatidiform mole are briefly analyzed.

All patients have been followed up for at least a year.

There have been 66 pregnancies subsequent to these moles, with 87 per cent eventuating in live births.

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TABLE I. PAIN

TYPE OF PAIN	NUMBER OF PATIENTS	PER CENT
Sharp, intermittent	43	46.00
Intermittent cramps	26	28.00
Stabbing pain with fainting	13	14.00
Pain in the shoulder	10	11.00
Dull ache	9	10.00
Labor pain	1	1.00
Sudden pain on defecation	2	2.00

(45 per cent) denied any amenorrhea, but upon careful analysis of the history of these patients, it was noted that frequently the menses had been scant or irregular. Sixty-four cases (71 per cent) complained of scanty bleeding; 10 cases (11 per cent) had continuous slight bleeding; three cases (4 per cent) had profuse bleeding; 13 patients (14 per cent) denied vaginal bleeding.

*Gastrointestinal Disturbance.*—Symptoms of gastrointestinal disturbance, which were present in 36 cases (40 per cent), consisted mainly of nausea and vomiting, for the major part induced by the abdominal pain. Diarrhea was noted in two cases (2.20 per cent).

*Abdominal Examination.*—Abdominal tenderness on palpation was noted in 74 cases (82 per cent); abdominal distention was recorded in five cases (8 per cent); rigidity and rebound tenderness was noted in 15 cases (16 per cent).

*Pelvic Examination.*—Pelvic examination was recorded in only 64 cases (71 per cent). Pain on motion of the cervix was present in 58 cases (90 per cent); adnexal mass was noted in 35 cases (55 per cent); a boggy mass in the post cul-de-sac was noted in 32 cases (50 per cent).

*Hematology.*—The leucocyte count was performed in 82 cases (90 per cent) on admission. Twenty-eight cases (34 per cent) had a leucocyte count of 15,000 or over. The highest leucocyte count recorded was 36,000. Those patients with active intraperitoneal hemorrhage usually had a high leucocyte count. Erythrocyte count was performed in 80 cases (88 per cent) on admission. Forty-six cases (58 per cent) had an erythrocyte count below 3.5 million on admission. The hemoglobin averaged 65 per cent in 80 cases.

*Friedman Test and Sedimentation Rate.*—Friedman tests were performed in eight cases. Seven were positive and one was negative. In the latter, clinical evidence indicated that we were dealing with an old ectopic pregnancy. Sedimentation rate was carried out in seven cases. Three patients with active intraperitoneal hemorrhage had a sedimentation rate over 50 mm. per hour.

*Hemoperitoneum.*—Free blood in the peritoneal cavity was present in 68 cases (75 per cent). The amount of blood present in the peritoneal cavity was not recorded in the majority of the cases.

*Type and Location of the Extrauterine Pregnancy.*—All of the extrauterine pregnancies were of the tubal variety except one, which was an abdominal gestation of six months' duration, the placenta of which was attached to the mesocolon. Fifty-five cases (61 per cent) of the tubal pregnancies were located in the right tube; 34 cases (39 per cent) in the left tube.

*Anatomic Findings.*—Table II shows that 60 cases (65 per cent) of the tubal pregnancies were located in the ampulla; 15 cases (17 per cent), isthmie; 1 case (1 per cent), interstitial; 13 cases (15 per cent), location not recorded. These figures are comparable to those reported by Langman.<sup>7</sup> In this series 51 cases (56 per cent) had ruptured tubal pregnancies.

*Surgical Procedure.*—Table III shows the various surgical procedures carried out in this series.

## EXTRAUTERINE PREGNANCY

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THIS study represents an analysis of 90 cases of extrauterine pregnancy, an incidence of 1.5 per cent of the total gynecologic admissions. The incidence recorded here is comparable to that recorded in studies by Graffagimino<sup>1</sup> and by Falk.<sup>2</sup> A survey of the literature of extrauterine pregnancy reveals that the majority of the published data was obtained from charity hospitals. This analysis differs from previous studies principally in two respects. First, that the cases presented were as a rule under observation by their family physicians for varying periods of time before admission, and therefore usually entered the hospital before becoming an emergency. Second, this study may more accurately reflect the usual diagnostic problems, the errors, and the expected clinical course than that of the aforementioned reports, since these cases are those of a moderate-sized voluntary hospital and were cared for by a relatively large number of physicians.

### Analysis of Material

*Age.*—Ages ranged from 19 to 43 years, the average being 30 years. Fifty-one cases (57 per cent) were between 25 and 34 years. These data correspond closely to those of Lisa<sup>3</sup> and Schumann.<sup>4</sup>

*Race.*—One patient was Negro, and the remaining 89 patients were white. In this hospital the ratio of Negro to white admissions is about 1 to 20.

*Parity.*—The incidence in relation to parity reveals that the largest group, 29 cases (32 per cent), occurred in patients with no previous pregnancies; 21 cases (22 per cent) with a history of one pregnancy; 16 cases (17 per cent) with two former pregnancies; eight cases (9 per cent) were pregnant three times; nine cases (10 per cent) gave history of more than four pregnancies; and in seven cases (8 per cent), the history of previous pregnancies was not recorded.

*Surgical History.*—A history of previous abdominal operation was present in 19 patients (20 per cent); six cases (6.6 per cent) had had previous ectopic pregnancy. One patient had had a previous tubal pregnancy four months prior to her second admission. (Smith<sup>5</sup> reported an incidence of 3.6 per cent second ectopic, and Weil<sup>6</sup> reported a figure of 1 per cent).

*Pain.*—The one constant symptom was pain, which was present in all of the 90 cases.\* The character of pain varied according to the pathologic findings. In the cases of ruptured tubal pregnancy, the pain was usually sharp or stabbing. The tubal abortions were usually accompanied by sharp, intermittent pain, while the unruptured tubal pregnancies were usually associated with dull ache. Table I shows that the classical history of stabbing pain and fainting was recorded in only 13 cases (14 per cent). Two cases complained of sudden pain on defecation.

*Menstrual Disturbance.*—Menstrual disturbance was one of the most common complaints, occurring in 84 cases (94 per cent). The disturbance was usually a period of amenorrhea followed by vaginal bleeding. Forty-one patients

\*In this series of patients, four presented more than one type of pain.

(12 per cent), and hysterectomy in only one case (1.2 per cent). Johnson,<sup>9</sup> however, reported in his series that unilateral salpingectomy was performed in 89 cases (77 per cent), appendectomy in 34 cases (29 per cent), and hysterectomy in 11 cases (9 per cent).

It is interesting to note that diagnostic colpotomy was not used in this series. It is well known that this procedure is of value only in the presence of hemoperitoneum, and often a long, stormy convalescence follows, and this may be the reason why the family physician is reluctant in performing a diagnostic colpotomy.

It is noteworthy that the mortality rate (2.2 per cent) reported here is considerably less than that reported by Ware<sup>10</sup> (5.41 per cent), and that of Lisa<sup>3</sup> (4.3 per cent), whose reports represent the findings of charity hospitals.

The lower mortality rate of a voluntary hospital may be due to several factors. Namely, the patients are admitted in better clinical conditions, and the family physician employs more conservative measures.

### Summary

1. Ninety cases of extrauterine pregnancy have been encountered in a voluntary hospital with a mortality rate of 2.2 per cent, from Oct. 1, 1939, to Oct. 1, 1945.

2. Symptoms of pain and some menstrual disturbance, usually amenorrhea followed by vaginal bleeding, were present in almost every case.

3. Abdominal pelvic examination gave valuable information.

4. In this series there were 89 tubal pregnancies and one abdominal pregnancy. The site of the tubal implantation was present most frequently in the ampullary portion, and least frequently in the interstitial.

The authors wish to express their indebtedness to Dr. Mark E. Maun, Associate Professor of Pathology at Wayne University, for his suggestions and invaluable aid in the preparation of this paper.

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TABLE II. LOCATION OF RUPTURED AND UNRUPTURED TUBAL PREGNANCY

LOCATION	NUMBER OF PATIENTS	PER CENT
Ampulla—abortion	25	27.00
Ampulla—ruptured	22	24.40
Ampulla—not ruptured	13	14.40
Isthmus—ruptured	15	17.00
Ruptured location not recorded	13	14.40
Interstitial—ruptured	1	1.00

TABLE III. STRUCTURES REMOVED AT OPERATION

STRUCTURES REMOVED	NUMBER OF PATIENTS
Unilateral salpingectomy	57
Bilateral salpingectomy	6
Salpingo-oophorectomy	8
Salpingectomy and appendectomy	7
Salpingo-oophorectomy and appendectomy	4
Bilateral oophorectomy and salpingectomy	2
Salpingectomy and curettage	3
Bilateral salpingectomy and hysterectomy	1
Salpingectomy, myomectomy, and plastic repairs of the tube	1

*Transfusion.*—Transfusion was done in 36 cases (40 per cent), eight times preoperatively, and the remainder during or after the operation. All of the patients received whole blood.

*Preoperative Diagnosis.*—Preoperative diagnosis was correct in 66 cases (73 per cent). This figure of correct diagnoses is in keeping with those reported by Schauffler<sup>8</sup> and Johnson.<sup>9</sup> This figure does not include conditions diagnosed as extrauterine pregnancy, which later proved to be incorrectly diagnosed. Incorrect diagnosis, under which extrauterine pregnancy was found at operation, included eight cases of ovarian cyst; seven cases of appendicitis; six cases of pelvic inflammatory disease; two cases of leiomyoma; and one incarcerated uterus.

*Mortality.*—In this series two deaths occurred, a mortality rate of 2.2 per cent. One patient with a right ruptured interstitial pregnancy was in shock on admission, and expired five hours after admission or one hour following surgery. Unfortunately she was not transfused. The other patient expired ten hours after admission. Her condition was satisfactory both before and immediately following surgery. An autopsy was not granted and we were unable to explain the cause of death.

### Discussion

In this survey as already noted, the cases presented were usually under observation by their family physicians prior to admission to the hospital; hence their clinical condition was better than those cases seen in charity hospitals. Only eight cases (9 per cent) were in shock on admission. Ware<sup>10</sup> reported in his series that 20 patients (22.2 per cent) were in shock on admission, and 11 cases (12 per cent) had an erythrocyte count below two million. In this study only a single patient (1.2 per cent) had an erythrocyte count below two million.

The physicians handling the cases reported here preferred conservative measures with their private patients. In this series of cases unilateral salpingectomy was performed in 82 cases (92 per cent), appendectomy in 11 cases



80/70. Treatment for shock was instituted. The patient rallied briefly, but soon the pulse and blood pressure were unobtainable. The clinical impression was "rapid internal hemorrhage;" "possible pulmonary thrombembolism."

*Postmortem Examination.*—The pathologic diagnosis was status following delivery induced by insertion of bougie in cervix; eclampsia; eclamptic lesions of the liver; subcapsular hemorrhage of anterior and superior surfaces of both hepatic lobes; rupture of capsule of superior surface of left lobe of liver; massive hemoperitoneum with blood clots over left lobe of liver; generalized pallor (anemia); hemorrhage of right rectus muscle; cerebral edema; regressive changes in tubular epithelium of kidney with slight fatty changes in glomerular tufts; slight hypertrophy of left ventricle; hyperemia and edema of lungs; edema of legs and retroperitoneal tissue, corpus luteum of pregnancy in left ovary, lactation hyperplasia of breasts, eosinophilic hyperplasia of anterior lobe of hypophysis, fibrous adhesive pleurisy of left side; cervical cysts; subserous leiomyomas of corpus uteri.



Fig. 1.—Undersurface of liver showing eclamptic hemorrhages.

*Description of Liver.*—The peritoneal cavity contained a large amount of bloody fluid. The liver projected beyond the costal margin. It weighed 2,800 Gm. The anterior surface of the right lobe showed a subcapsular hemorrhage 19 by 15 centimeters. Its margins were 4 to 7.5 cm. from the superior edge of the lobe; 0.9 to 3 cm. from the lateral edge; and 0.7 to 2 cm. from the inferior edge. The hemorrhage extended to involve the anterior and superior surface of the left lobe. Here the hemorrhagic area measured 17 by 12 centimeters. Its margins were practically flush with the left lateral edge; and 3.1 cm. above the left inferior edge. In the superior surface of the left lobe of the liver the capsule was torn; there was a denuded area 4 by 2.1 cm., over which lay blood clots. The subcapsular hemorrhage measured 2.3 cm. in depth. The remaining surfaces of the liver and its parenchyma was splotted with hemorrhages. The parenchyma was yellow in color. Lobular markings were not clearly seen. Microscopically the liver showed typical eclamptic lesions with recent subcapsular hemorrhage and capsular rupture. Eclamptic lesions were present in relation to the subcapsular hemorrhage.

## SPONTANEOUS RUPTURE OF THE LIVER IN ECLAMPSIA WITH FATAL HEMOPERITONEUM

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**S**PONTANEOUS rupture of the liver is a rare lesion. Its occurrence in connection with pregnancy has been reported in only a few isolated cases. We present the clinical and postmortem findings in an eclamptic patient with spontaneous rupture of the liver and massive hemorrhage into the peritoneal cavity following induced labor and delivery.

*Clinical History.*—A 26-year-old Negro woman, para iii, gravida iv, was admitted to the Edward J. Meyer Memorial Hospital Dec. 25, 1944, with convulsions. She died Dec. 27, 1944.

The date of the last menstrual period could not be ascertained. The expected date of delivery was some time in February, 1945. Prenatal care had consisted of one visit to a physician in October, 1944.

For two and a half hours before entry to the hospital, the patient had four convulsions, each of five minutes' duration. Other complaints included blurring of vision with spots before the eyes, and swelling of the ankles.

On examination, the patient was a well-developed and obese Negro woman, acutely ill. The blood pressure was 200/145. The uterus was enlarged to the size of a seven months' pregnancy. No fetal heart sounds were heard. There was dullness in both flanks. The ankles showed 4 plus edema. On rectal examination, no presenting parts were palpated. The cervix was long and firm; it was not dilated.

*Laboratory Data.*—Urine: specific gravity 1.025; albumin 4 plus; sugar 0; sediment negative. Wassermann test was negative.

*Course.*—During the first day in the hospital, the patient continued to have convulsions and emesis. She was treated with intravenous glucose and magnesium sulfate, morphine, and a salt-free diet. On Dec. 26, 1944, at 2:15 P.M. the patient was taken to the lying-in room. A sterile bougie was inserted through the cervix. The vagina was packed with sterile gauze. The membranes ruptured toward the end of the procedure. Subsequently, the patient was given intranasal pitocin. Convulsions and emesis stopped. The blood pressure was 205/130.

On Dec. 27, 1944, at 3:05 A.M., the patient had one strong sustained contraction and precipitated the vaginal pack, bougie, and a female infant weighing 2 pounds, 2 ounces from a vertex presentation. The perineum was intact. The secundines\* were expressed completely with the baby, who cried and breathed spontaneously.†

Following the precipitate delivery, the patient appeared drowsy. Diarrhea developed. The pulse rate and temperature rose. The blood pressure was 195/145. The uterine fundus was firm.

At 7:00 P.M. the patient rapidly became pale and dyspneic. In a short time the abdomen was distended. A fluid wave was elicited. The blood pressure was

\*The placenta and cord weighed 300 Gm. The insertion of the cord was marginal. The placenta measured 13 by 15 cm. in length. It showed no infarcts.

†The infant lived about twenty-four hours. Its weight was 920 Gm.; its length, 34 cm. At autopsy, the findings included prematurity, partial pulmonary atelectasis with aspirated material in alveoli, and petechial hemorrhages in epicardium.

reasonable to assume that the eclamptic lesions could be the sole cause, other factors which might have precipitated the extensive subcapsular hemorrhage and capsular rupture must be considered. These include convulsions, vomiting, and parturition. In all three, the intra-abdominal pressure rises. There are powerful contractions of the abdominal muscles. In vomiting and parturition, particularly, the diaphragm contracts and descends sharply and deeply. The liver is depressed and compressed. Flexion of the body during emesis and convulsions brings the liver into relation to the rigid costal margin and spine. An enlarged liver with damaged parenchyma is conceived to be less resistant to mechanical effects withstood by a normal organ. Of interest in our case was the limitation of the subcapsular hemorrhage to the anterior and superior surfaces of the liver, despite the fact that eclamptic hemorrhages were abundant beneath the capsule of all surfaces. Might this anterosuperior distribution of the subcapsular hemorrhage suggest the influence of the precipitating factors under discussion, especially in respect to contraction of abdominal muscles and diaphragm, and to rigidity of costal margin, and be related to their effects?

If we accept the premise that convulsions, vomiting, and parturition, could have precipitated subcapsular hemorrhage with capsular rupture in the eclamptic liver of this patient, the question arises whether we can evaluate how much of a part any of these factors played in helping to produce the subcapsular lesion. Certain clinical and pathologic data can be adduced in attempt to form an answer. Up to, and after the time convulsions and emesis stopped, the patient complained of no pain in her abdomen. The blood pressure remained high. It was following delivery with a strong sustained contraction that the patient became drowsy. Then the pulse rate and temperature rose. Diarrhea developed. Sixteen hours later the patient rather rapidly went into collapse and died in a short time, so that the impression of the physician was "rapid internal hemorrhage." Upon the time-relationships of the clinical data, it seems justifiable to speculate that the subcapsular hemorrhage occurred more or less concomitantly with delivery, finally to be complicated by rupture of the capsule over the superior surface of the left lobe of the liver with excessive bleeding into the peritoneal cavity. Microscopic examination of the liver speaks for a recent subcapsular hemorrhage.

Thus far we have assumed the subcapsular hemorrhage and capsular rupture in our case to be spontaneous in origin, because no definite history of significant external trauma to the abdomen was present. In all honesty it should be noted that movements and manipulations to which an ordinary patient is subjected without danger—e.g., transportation from one place to another, palpation, and percussion during physical examination—might possibly prove sufficient to cause subcapsular hemorrhage and rupture of the liver in a patient with an enlarged, tense, damaged organ. The skin and subcutaneous tissue of the abdomen in our case showed no visible effects of trauma. The right rectus muscle revealed a hemorrhage which, on microscopic examination, proved to be a hemorrhagic necrosis associated with regressive and inflammatory changes in the vessels, apparently of eclamptic origin.

From the available literature, we have abstracted five cases of presumably spontaneous rupture of the liver in pregnancy with hemorrhage into the peritoneal cavity.

Kolosoff (1914).<sup>1</sup> A 39-year-old primipara, had severe eclampsia. At the onset of anesthesia for a vaginal cesarean section, the patient collapsed. In the interest of the child, a classical section was carried out. The peritoneal cavity showed extensive hemorrhage. A deeply asphyxiated infant with secundines was extracted from the uterus. The source of the hemorrhage was a necrotic focus on the superior surface of the left lobe of the liver which showed typical eclamptic lesions. The operation was completed on the dead patient.

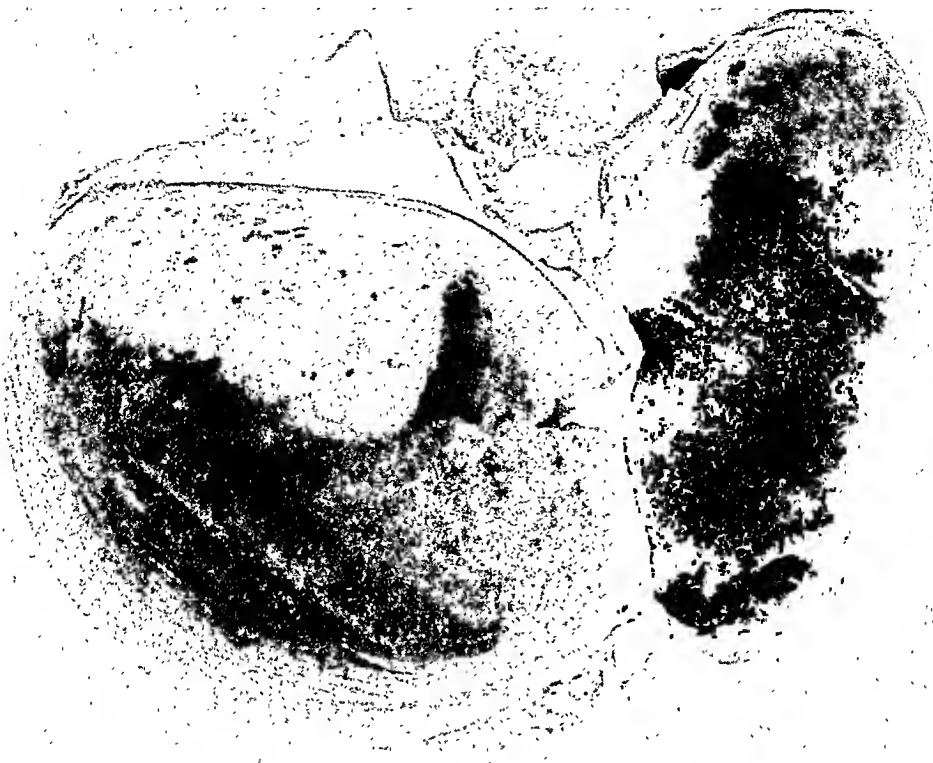


Fig. 2.—Anterior and superior surfaces of liver showing subcapsular hemorrhage.



Fig. 3.—Cross section of liver showing subcapsular hemorrhage.

### Discussion

On the basis of the obstetric and postmortem findings, our case was one of eclampsia in the seventh month of pregnancy, with a rare fatal complication. The immediate cause of death was massive hemorrhage into the peritoneal cavity from rupture of the liver associated with subcapsular hemorrhage.

Undoubtedly, the eclamptic lesions in the liver constituted the primary cause for the subcapsular hemorrhage and capsular rupture. Although it is

## UMBILICAL ACCESSORY LIVER

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**H**ERNIATION of liver into the extraembryonic, celomic cavity of the umbilicus, with or without other portions of the viscera, is extremely rare, and only seven valid cases have been reported in the literature.

In 1903, Sanderson<sup>1</sup> saw a newborn baby twelve hours after birth, apparently suffering from an amniotic hernia. All of the abdominal organs could be seen through the thin, transparent covering which had already begun to dry. Although Sanderson felt that the opportune time for repair of the defect had passed, nevertheless, he advised an operation as a last resort. A marked protrusion already had been produced from the abdominal pressure, and half of the liver had to be resected before it could be replaced in the abdominal cavity in order to bring the muscles and skin together. The baby died twenty-four hours later. Sanderson stressed that the time to operate in such a case is immediately after birth, before the thin, membranous covering of the abdominal wall is dried out, and before the hernial protrusion has increased in size by the accumulation of fluid in the stomach.

In 1905, Stewart<sup>2</sup> reported the case of a well-developed male child with a hernia of the cord the size of a very large apple, which contained the liver and a portion of the intestine. The cord dropped off at the usual time, leaving the sac exposed. A plastic operation was attempted, but the whole of the liver was so adherent to the apex of the sac that its separation was impossible.

Hipsley<sup>3</sup> reported a case in 1925 of a total spherical herniation of the liver into the cord of a male infant. It was reduced surgically twelve hours after birth, and the baby made an uneventful recovery.

In 1941, Sanford<sup>4</sup> reported a case of total herniation of the liver into the cord with the complete recovery of the baby. He stressed the importance of an early operation, allowing twenty-four hours for the baby to recover from the stresses of parturition.

In the same year Searle and Engle<sup>5</sup> discussed a case of herniation of the entire liver, stomach, gall bladder, and large and small intestines, and mentioned that the only treatment was surgery to be done immediately, as all unoperated patients usually die from peritonitis or paralytic ileus.

In 1944, Casey<sup>6</sup> presented a case of a newborn in which the entire liver was situated in an umbilical sac. The other organs were in their normal location. Surgery was performed four hours after birth with successful results.

The above six cases show herniation of the entire liver; whereas, in the case being presented, separate liver tissue was found in the normal liver location as well as in the extraembryonic celomic cavity near the fetal end of the umbilical cord.

The seventh case reported by Morgagni,<sup>7</sup> and abstracted below, is similar to our case. Upon checking Morgagni's original report, we find that our translation differed from Thomas A. Cullen's making our case the second instead of the original case reported. Our abstract is as follows:

"A paraumbilical tumor, the size of a fist, was seen in a newborn child, born of healthy parents who had other healthy children. The tumor was livid and covered with gangrenous cicatrix. It looked like an umbilical hernia with intestinal contents, including liver. The baby died on the thirty-fifth day after birth.

Herz (1918).<sup>2</sup> A 41-year-old multipara in the eighth month of pregnancy developed severe pain under the right costal margin accompanied by air hunger and emesis. The clinical impression was "gallstone colic." Fetal heart sounds were not heard. The urine showed albumin. When collapse of the patient followed, internal hemorrhage was diagnosed. A postmortem cesarean section was performed. Autopsy disclosed eclampsia with subcapsular hemorrhage on anterior surface of right lobe of liver with a tear near the gall bladder, and with peritoneal hemorrhage.

Duverges (1928).<sup>3</sup> A 39-year-old multipara had eclampsia with convulsions. Suddenly she went into collapse, with pallor and abdominal pain. Fetal heart sounds disappeared. At autopsy there was hemorrhage in the peritoneal cavity and retroperitoneal space, the source of which was subcapsular hemorrhage in an eclamptic liver.

Roemer (1941).<sup>4</sup> A 30-year-old multipara, who had complained of headache for a few weeks, suddenly experienced sharp pain below the right costal arch. The clinical impression was "gall bladder attack." Then the patient had eight convulsions. Fetal heart tones were heard. The patient responded to treatment for eclampsia. Ten minutes after she was moved to another room, the patient went into collapse and died shortly. At autopsy, the chief diagnosis was eclampsia with subcapsular hemorrhage of right lateral surface of liver and with hemorrhage into the peritoneal cavity.

Rademaker (1943).<sup>5\*</sup> A 32-year-old toxemic patient with a progressively rising blood pressure was transferred to a hospital in the eighth month of pregnancy when she began to vomit. After admission the patient went into collapse with a dull ache in the right upper quadrant. Labor had not commenced. Fetal heart sounds were absent. The clinical impression was ruptured uterus. At laparotomy extensive peritoneal hemorrhage was found. Following a Porro operation, which yielded a dead immature fetus, the source of the hemorrhage was found to be a tear in the right lobe (apparently anterosuperior surface) of the liver over an area of mushy tissue, about the size of a grapefruit. The torn mushy area was packed. Three months after operation, attended with a stormy convalescence, the patient was healthy; the blood pressure was 145/90.

In summary, all of the five cases of rupture of the liver in pregnancy with hemorrhage into the peritoneal cavity occurred in eclampsia. No patient had a definite history of abdominal trauma. In two cases the clinical picture of rupture and hemorrhage appeared after transportation of the patient. Convulsions were present in three cases. Pain in the right upper quadrant was a common symptom. Shock supervened. Fetal heart sounds disappeared. The anterolateral-superior surfaces of the liver were always involved. In three cases, rupture of the liver occurred from diffuse subcapsular hemorrhage; in two cases, from necrotic foci. Four cases terminated fatally. In one patient operation was carried out with recovery.

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\*Rademaker cited Abercrombie's case (1847) of rupture of the liver in pregnancy, which has suggestive history of an external traumatic factor.

quadrate lobe appeared to be completely separated from the rudimentary left lobe by the ductus venosus, quite some distance from the caudate lobe. There was no caudate process, so that the lower margin of the caudate lobe was free. A portal vein extended between the right and left lobes on the anterior surface. There were sutures about the left branch of the portal vein and the hepatic artery on the undersurface of the liver in situ. The left branch of the hepatic vein followed the anterior portion of the liver instead of the normal posterior and emptied into the inferior vena cava. The two vessels on the anterior surface, near the falciform ligament, were probably a branch of the portal vein and the hepatic artery. The accessory lobe formed a triangular mass which measured 3 by 2 by 2 centimeters. Extending out to the right of the falciform ligament and to the left of the accessory lobe, which might have been the quadrate lobe, was the gall bladder, 3 cm. in length and twisted upon itself.



Fig. 2.—Formalin fixed liver sectioned. A. Tied off cord. B. Receptacle containing bile. C. Thick capsule about the liver. D. Large vessel entering the liver. E. Areas of colloid cystic degeneration.

The right lung weighed 24 Gm. and had four lobes. The left lung weighed 19 grams. Many solid portions were present at the base and posterior portions of the lung. No abnormalities were found in any of the other organs.

The microscopic examination of the mass revealed neonatal liver tissue. The markedly thickened capsule showed an edema and a dense neutrophilic exudation extending into the portal system and separating the liver cords. The hepatocytes were enlarged, granular, and edematous. Degeneration was more extensive near the periphery. There was a marked engorgement of the sinusoids, and comparatively little degeneration of the liver was also found in the usual anatomic location. The abdominal wall was closed in layers.

The baby's immediate postoperative condition was good. Thirty milliliters of the mother's blood was injected into the right buttock about one-half hour after operation. Physiologic salt solution and coramine were given parenterally every half hour after the operation. Oxygen was given continuously. The rectal temperature dropped to 95.4° F. before expiration, twenty-nine hours after surgical intervention.



"A duplicate liver was found in the normal location after dissection of the abdomen. It was smaller than the herniated liver and was connected with it by a thick membrane which contained the portal and hepatic veins and the hepatic artery. The internal liver was divided into several lobes, and the gall bladder was absent."

Morgagni proposed an hypothesis that the duplicated liver could be the result of a twin pregnancy in which only the liver remained, the other parts of the twin fetus having perished in the uterus. Morgagni also quoted a report by Zambeccarius of twins with connected livers and anterior abdominal walls.

### Case Report

The case that we are presenting is that of a white baby girl born at the Frank Cuneo Hospital on Dec. 10, 1942, having a congenital malformation of the cord. The baby weighed 2,842 Gm. (6 pounds, 4 ounces). The parents' history revealed no relevant information. The mother had given birth to a healthy boy seven years previously, after a short period of labor.

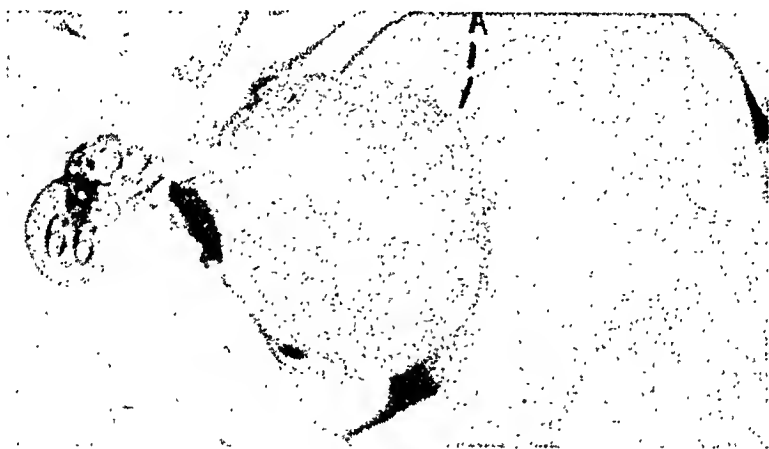


Fig. 1.—View of mass protruding into the umbilical cord.

A large pyriform, yellowish-green mass, breaching the abdominal wall and measuring 7.5 by 7.0 cm. in diameter, protruded just above the umbilical ring. The dilated cord joined the raised skin on the baby's abdomen and was covered with a membrane resembling tissue paper (Fig. 1). The distended portion of the cord was translucent and flatulent, and did not communicate with the peritoneal cavity, except for the passage of blood vessels and possibly a biliary tract.

Blood examination revealed: Hemoglobin, 74 per cent (11.5 Gm.); erythrocytes, 3,500,000; leukocytes, 11,400; coagulation time, three minutes; Rh factor, negative. The baby regurgitated most of its food prior to the operation, which was performed forty-eight hours after delivery under an ethylene anesthesia.

A circular incision was made which extended from the skin through the peritoneum. Grossly, the sac contained a gelatinous substance (Wharton's jelly), a structure which resembled liver substance, and a vesicle containing a mucinous bile. No intestines were found in the sac. There was no connection between the sac and the peritoneal cavity, except the blood vessels which were ligated. A nearly normal-sized liver removed at the autopsy measured 6.5 by 5 by 4 centimeters. Along the lower border of the right lobe of the liver was a fissure 2.5 cm. in length, which extended into the liver for a distance of 6 millimeters. The left lobe was rudimentary, and was separated from the right lobe by an irregular but intact falciform ligament. On the posterior surface the



The etiology of the ectopic liver may be explained that when the vitelline duct retracted into the extraembryonic cavity of the cord during the sixth and seventh weeks, the large and freer left portion of the liver may have become attached to the enveloping mesentery and drawn into that cavity where it developed. The falciform may have been the link of attachment to form the ligamentous trunk. The fact that the vessels entered the anterior rather than the posterior surface would support the view that the trunk was under pressure from a frontal pull, or that cleavage had taken place in order to have the hiatus in front, for these vessels are commonly found on the posterior inferior surface. The biliary remained in situ.

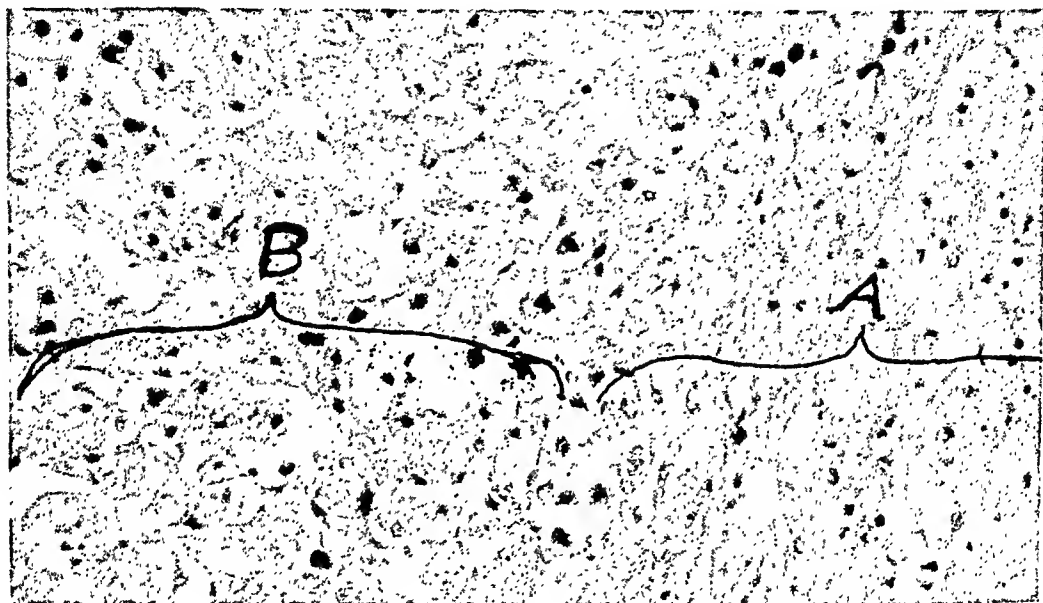


Fig. 4.—Microscopic section of liver found in the umbilical cord. A. Thickened capsule. B. Reveals the degeneration in the liver cells.

To further support the above theory, it is known that, at the end of the eighth week, the diaphragm is completed and has completed its descent. In the ninth week, when the liver<sup>12</sup> has reached its greatest relative size, the intra-abdominal pressure may have forced the freer portion into the extraembryonic celomic cavity. Additional weight is lent to this hypothesis in our case in that the total liver tissue, even after birth, weighed about two-thirds more than normal. It is, therefore, probable that the liver, having been under abnormal pressure between the ninth and tenth weeks, was forced into the only unopened avenue of escape, the space in the cord from which the intestines were withdrawn. There is no known mechanism to withdraw the liver as in the rotation of the returning bowel and, consequently, it had to develop in the cord. The pressure of the rectal muscles would offer more resistance than that of the umbilicus, thereby, forcing it to grow out and form a pedicle by pressure of the rectal muscles. This agrees with the theory of Morgagni, Sanford, Arey,<sup>11</sup> and Bartlemetz.<sup>13</sup> This theory is further supported by Sanderson's case, in which he had to resect half of the liver in order to effect a closure of the abdomen.

Jaquemet<sup>9</sup> stated that a double liver was never encountered except in double monsters; and, even in subjects when there is a deviation from the normal embryonic development, the liver is invariably present and stable.

Trimingham and his co-workers<sup>10</sup> stated that "the treatment of choice is surgical, and prognosis in the individual case depends largely on how soon after birth, in terms of hours, operation is undertaken."

The gross examination of the hernial sac revealed that the entire mass with its coverings weighed 67.5 grams. It was fluctuant on one side. The external covering resembled tissue paper. The inner covering was thick, rather soft, and gelatinous on one side. The fluctuant portion contained fluid similar to bile. Grossly, the sac had the appearance of a gall bladder, and the fluid within was proved to be bile. The mass, after fixation in formalin, resembled a greenish liver with grey areas of degeneration and a few circular areas filled with homogeneous colloid. The largest cyst measured 11 mm. in diameter. A thickened vessel, filled with blood, entered the liver substance. The sectioned mass revealed a cordlike structure extending into the liver tissue and connected by the umbilical cord on one end, and probably extending to the anterior surface of the liver in situ (Fig. 2).

Harvey<sup>14</sup> was of the opinion that the sac containing bile was large enough to contain all the bile secreted by a neonatal liver.

The postmortem examination showed that the inner peritoneal cut was slightly roughened but completely covered over. The liver extended 2.5 cm. below the costal margin and weighed 52.5 grams. The mass which was removed surgically weighed 67.5 grams. The liver cords stained poorly as compared with those found in situ.

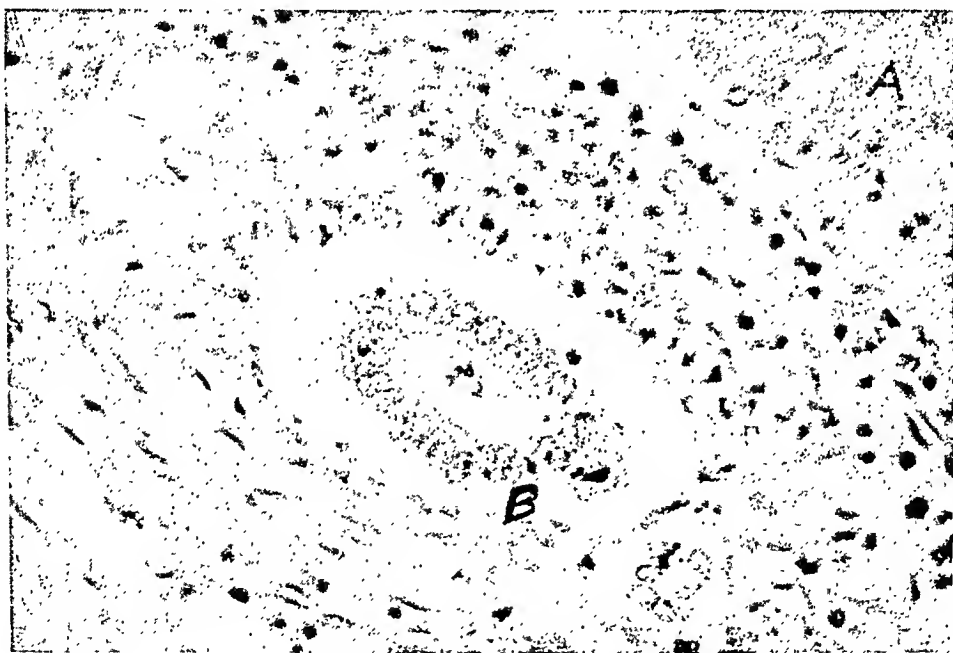


Fig. 3.—Microscopic section of the liver. A. Liver cords. B. Biliary duct surrounded by fibrous tissue with some inflammatory cells.

Liver buds are evident at three and one-half weeks in the human embryo as they first arise as a diverticulum between the fore- and mid-gut next to the pericardium. The hepatic diverticulum extends into the mesenchyme of the septum transversum between the pericardial cavity and the yolk stalk. The right and left lobes are discernible at six weeks, when the embryo is 12 mm. in length. Normally the intestinal loops are herniated into the umbilical cord between the seventh and tenth weeks of intrauterine life.

Cullen's<sup>8</sup> dictum states that liver cannot survive unless there is a rich blood supply for its existence, namely, arterial and portal, with venous as well as biliary drainage. In this case, the drainage was limited to a sac just outside of the liver, which Harvey maintained was large enough to store all the bile secreted in a neonatal liver.

## SLIDING HERNIA OF THE FALLOPIAN TUBE

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A SLIDING hernia may be defined as a hernia in which a part of the sac wall is made up of a portion of a retroperitoneal viscus. Most commonly, the ascending or descending colon are the organs involved in such a hernia. A. V. Moschowitz stated, "the relative frequency of the organs involved in a sliding hernia is roughly inversely proportional to the amount of peritoneal covering."<sup>1</sup> Based on this idea, he placed the abdominal organs in groups according to their likelihood of entering into the formation of a sliding hernia (Table I).<sup>2</sup> A review, to date, of the reported cases of sliding hernia of the

TABLE I. THE ABDOMINAL ORGANS IN GROUPS ACCORDING TO THEIR LIKELIHOOD OF ENTERING INTO THE FORMATION OF A SLIDING HERNIA\*

ALWAYS	NEVER	RARELY	LIKELY
Ureter	Ovary	Sigmoid flexure	Ascending colon
	Stomach	Small intestine	Descending colon
	Liver	Uterus	Broad ligament
	Spleen	Fallopian tube	Bladder
	Transverse colon		Appendix
	Cecum		
	Omentum		

\*Table reprinted by kind permission of J. B. Lippincott Co. from article, "Hernia of the Large Intestine with special reference to Sliding Hernia." Moschowitz, A. V.: *Ann. Surg.* 37: 611, 1914.

various abdominal organs with reference to their relative frequency of occurrence bears out the soundness of the theoretical basis of this grouping. Only one case of sliding hernia of the Fallopian tube has been reported. That case was described in 1920 by McNealy,<sup>3</sup> and is strikingly similar to the case herein to be reported.

### Case History

Mrs. E. S., a widow, aged 41 years, entered the hospital on July 7, 1941, with the complaint of a "lump" in the left inguinal region of eight years' duration. The mass was painless until two years before, at which time an increase in its size was noted and a dragging sensation was felt when lying down, more pronounced when the patient lay on her right side. There was no recollection of the mass reducing itself, nor was reduction attempted. The past history was essentially normal, except for the excision of a benign breast tumor three years before. The menses were regular every twenty-eight days, with a scant flow of two to three days' duration. General physical examination was unimportant, except for the finding of a mass approximately 2½ by 1½ inches in diameter in the left labium, which gave an impulse on coughing. The mass was not easily reducible, and did not transilluminate. Vaginal examination revealed a normal-sized uterus pulled over to the left side.

*Operation.*—Under gas-oxygen-ether anesthesia, a left inguinal incision parallel to Poupart's ligament was made. The inguinal canal was exposed after splitting the external oblique fascia. The round ligament was isolated. There was a lipoma on its lateral side. A hernial sac was closely adherent and

It is the consensus of opinion that surgical intervention should be undertaken in all of these cases as soon after birth as feasible, calculated in hours rather than days, because of the inflammatory and necrotic changes described above. This school of thought is supported by Sanderson, Sanford, Searle, and Engmire, and Trimmingham and his associates.

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ment unfolds to become the parietal peritoneum over the lateral pelvic wall it covers the site of the internal ring. The ovary and infundibulum (fimbriated end) overlie the region of the internal ring.

When a hernia develops at the internal ring, the parietal peritoneum that enters into the formation of its posterior wall is not only in direct continuity with the anterior peritoneal layer of the broad ligament, but also immediately adjacent to it (Fig. 1). If now it is assumed in this case, as it is in sliding hernias of the large intestine, that a very loose connection exists between the peritoneal layers of the broad ligament, the pulling mechanism of the hernia

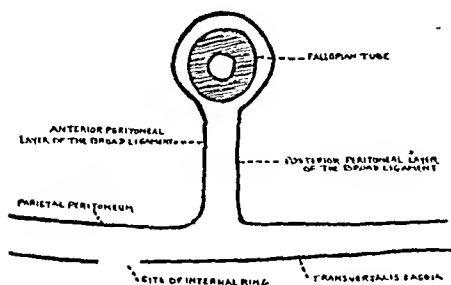


Fig. 1.—First stage in development of sliding hernia of the Fallopian tube. Paramedian sagittal section of pelvic inguinal region viewed from the left side showing the proximity of the internal ring to the broad ligament.

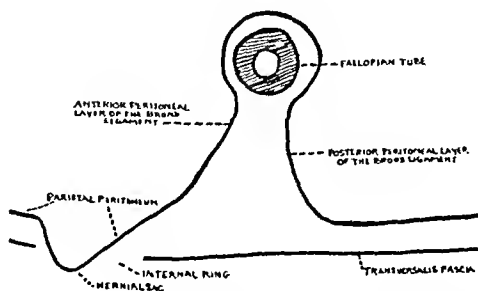


Fig. 2.—Second stage in the development of sliding hernia of the Fallopian tube. The leaves of the broad ligament are being separated and the connection of the anterior peritoneal layer of the broad ligament to the posterior wall of the hernial sac is shown.

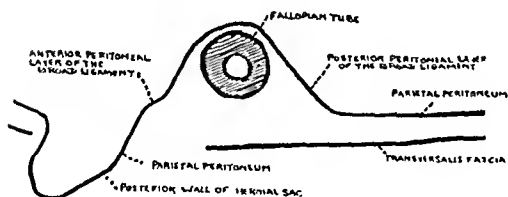


Fig. 3.—Third stage in the development of sliding hernia of the Fallopian tube. The inferior portion of the anterior peritoneal layer of the broad ligament is now at the internal ring and makes up the uppermost portion of the posterior sac wall.

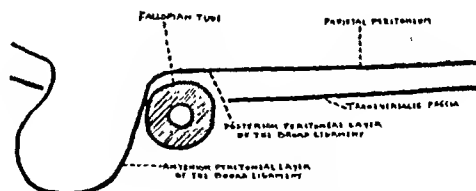


Fig. 4.—Fourth stage in the development of sliding hernia of the Fallopian tube. The leaves of the broad ligament have been completely separated. The anterior peritoneal layer of the broad ligament is entirely on the posterior wall of the hernial sac. The enclosed tube is at the uppermost portion of the posterior sac wall at the site of the internal ring.

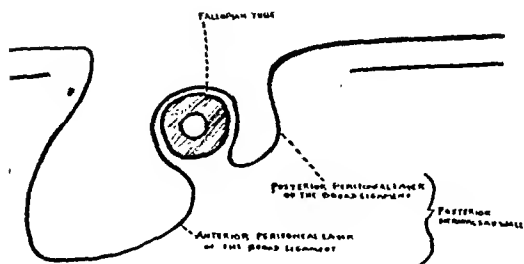
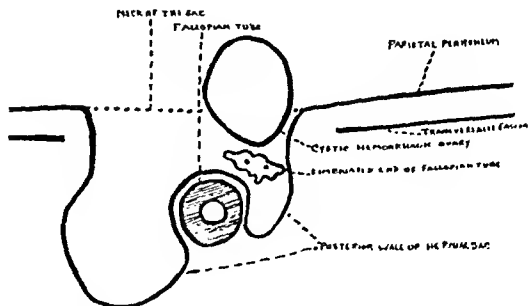


Fig. 5.—Final stage in the development of sliding hernia of the Fallopian tube. The anterior and posterior peritoneal layers of the broad ligament with the enclosed tube have become part of the posterior wall of the hernial sac.

Fig. 6.—Sagittal section of sac and contents as found at operation. The Fallopian tube is part of the posterior sac wall. The cystic hemorrhagic ovary is within the lumen of the sac at the site of the internal ring. The fimbriated end of the tube is within the lumen of the body of the sac as one of its contents.



posterior to the round ligament. The hernial sac in its distal portion was bilocular. One component was medial to and the other lateral to the round ligament. The two locules joined together in a common body and neck. On opening the sac, a tubular mass presented on the posterior wall. This was identified as the Fallopian tube when the fimbriae and a cystic hemorrhagic ovary presented at the neck of the sac. Under the impression that the tube was adherent, an effort was made to free it from the posterior wall of the hernial sac. This procedure gave rise to brisk bleeding, which was controlled by packing. In the face of these unusual findings it seemed expedient to expose the pelvis. The opening in the peritoneum at the internal ring was then extended upward after splitting the transversalis fascia, the transversus, and internal oblique muscles.

On exposure of the pelvis, it was noted that the fundus of the uterus lay close to the left lateral pelvic wall, and that the left broad ligament was missing. The uterine end of the left Fallopian tube was the only portion of the broad ligament within the pelvic cavity. The rest of the tube appeared to enter the internal ring on the posterior wall of the hernial sac. The cystic hemorrhagic ovary and fimbriated end of the tube were within the lumen of the internal ring.

The Fallopian tube was transected at its uterine end. The left ovary was removed after clamping, cutting, and ligating the mesovarium. The Fallopian tube and its fimbriated end were removed with the transection of the sac at the site of the internal ring. The internal ring and the peritoneum incised above it were closed with interrupted silk sutures. The severed transversus and internal oblique muscles were then sutured. A typical Bassini repair followed. Silk sutures were used throughout. The convalescence was uneventful.

### Discussion

The formation of a sliding hernia of the Fallopian tube is not difficult to appreciate when the anatomy of the pelvic inguinal region is reviewed.<sup>4, 5</sup>

The broad ligament is covered on its anterior, posterior, and superior surfaces by peritoneum. Medially the peritoneum on these surfaces spreads out to be continuous with the peritoneum covering the uterus. These layers are spread out on the lateral pelvic wall to become continuous with the parietal peritoneum covering the iliac vessels. Inferiorly the layers diverge to form the peritoneal surfaces of the anterior and posterior cul-de-sacs.

The Fallopian tube, except for its lateral fifth, is a retroperitoneal viscus lying in the superior border of the broad ligament. It is completely covered by peritoneum on its anterior, posterior, and superior surfaces. Its inferior surface is connected with the retroperitoneal space in the broad ligament.

The lateral fifth of the uterine tube, known as the infundibulum (fimbriated end), does not truly lie between the layers of the broad ligament. It may be considered to sprout out from the lateral end of the superior border of the broad ligament, completely investing itself with peritoneum. The ovary, in similar fashion, is completely invested by peritoneum and connected to the broad ligament by a pedicle derived from the posterior surface of the broad ligament, and known as the mesovarium. The superior portion of the lateral fifth of the broad ligament that extends from the lateral end of the ampulla of the tube and mesovarium to spread out on the lateral pelvic wall is known as the infundibulopelvic ligament. As the anterior layer of peritoneum of this liga-

# Department of Reviews and Abstracts

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## Selected Abstracts

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### Cesarean Section

Lopez Monti, Ricardo: Intraperitoneal Sulfonamide Therapy in Cesarean Operations on Contaminated Cases, *An. d. Inst. matern. y asist. social*, Buenos Aires 5: 170, 1943.

The author reports fifteen contaminated cases which were treated by low cesarean section and intraperitoneal sulfonamide therapy, according to the method of Perez and Echevarria. Great care must be taken to: (1) avoid the introduction of amniotic fluid into the peritoneal cavity, which can be accomplished by making a small opening in the uterus through which the amniotic fluid can readily be aspirated; (2) spread the 4 Gm. of sulfanilamide over the peritoneum, since this serous membrane provides the best absorption as compared with other routes of introduction and permits the highest drug concentration in the local blood vessels surrounding the septic focus; (3) suture the walls in five layers and the aponeurosis with chromic catgut, with the view of early mobilization of the patient without danger of evisceration.

The mortality among the fifteen cases was zero and the morbidity rate was  $7\frac{1}{2}$  per cent. Sulfanilamide was used in twelve cases; sulfapyridine in two; and sulfachrysoidine in one (the latter being the only case in which complications occurred). The author concludes that provided the operation is done early, and the indications are followed, the results are such as to justify the statement: "the problem of cesarean operation of the contaminated case has positively been solved." Moreover, this method should be used whenever the delivery through the normal route endangers the life of the mother or child. It diminishes the indication for symphysiotomy. The state of the excretory organs and liver must, however, be investigated because a lesion of these organs is a contraindication to the use of sulfa drugs or suggests reducing their amount. In such cases, supportive treatment should be given with vitamins, liver extract and large doses of salt and sugar solution. The analgesic effect of the sulfonamides has also been demonstrated, owing to which sedatives need not be administered. Deep respiration is advised, and early mobilization prescribed, to obviate the danger of pulmonary congestion and embolism.

J. P. GREENHILL.

### Endocrinology

Perez, Manuel Luis: Hyperthyroidism in Women and in Pregnancy, *An. d. Inst. matern. y asist. social*, Buenos Aires 5: 9, 1943.

The author states that the reciprocal relationship between the thyroid and gonadal glands in the female has been amply demonstrated both clinically and experimentally. Puberty, for instance, modifies the function of the thyroid gland causing its enlargement during the days preceding menstruation. Aside from this physiologic hypertrophy, it may produce pathologic changes ranging from simple goiter to true thyrotoxicosis. Conversely, pre-existing hyperthyroidism may influence the pubertal period, in delaying the first appearance of menstruation and causing subsequent menstrual irregularities. Cases of thyroprivous metrorrhagia, on the other hand, were described by Kocher. True Basedow disease

will unfold the layers of the broad ligament and draw them into the formation of the posterior wall of the sac. The Fallopian tube enclosed between the layers of the broad ligament will therefore be part of the posterior surface of the hernial sac. The various stages in the formation of the sliding hernia of the fallopian tube are illustrated in the accompanying series of diagrams.

Fig. 2 shows the leaves of the broad ligament being separated by the pulling mechanism of the hernial sac. The direct and immediate connection of the posterior wall of the hernial sac with the parietal peritoneum and anterior peritoneal layer of the broad ligament is illustrated.

In Fig. 3 the parietal peritoneum between the anterior peritoneal layer of the broad ligament and the internal ring has been pulled down to make up part of the posterior wall of the hernial sac. The leaves of the broad ligament are almost completely unfolded and the anterior peritoneal layer is now at the internal inguinal ring and makes up the uppermost portion of the posterior wall of the hernial sac.

Fig. 4 shows the entire anterior peritoneal layer of the broad ligament as part of the posterior surface of the hernial sac. The Fallopian tube is now located at the site of the internal ring.

The final stage in the development of the sliding hernia of the Fallopian tube is illustrated in Fig. 5. The posterior peritoneal layer of the broad ligament now occupies approximately the upper half of the posterior wall of the hernial sac. The enclosed Fallopian tube occupies the midposition of the posterior wall.

Fig. 6 is a sagittal section of the hernial sac as found at operation. It is to be noted that the ovary and fimbriated end of the tube are contents of the sac whereas the ampulla of the Fallopian tube is part of the posterior wall of the hernial sac and constitutes a sliding hernia of this organ.

### Comment

Graham has called attention to the unusual amount of fat present about the sac in sliding hernia after the inguinal canal is opened.<sup>6</sup> A moderate-sized lipoma existed in this case.

A bilocular sac frequently occurs in the unusual forms of hernia—most consistently in the relatively rare interstitial hernia.<sup>7</sup> The significance of the bilocular sac in this case is open to conjecture.

In retrospect, the history of dragging pain on lying on the right side plus the fact that the uterus was drawn and apparently fixed to the left side of the patient should have made one consider the possibility of the tube and ovary being involved in the hernial sac.

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de Moracs, A.: Radiologic Aspects of Ectopic Pregnancy, An. brasil de ginec. 9: 343, 1944.

The author employed hysterosalpingography in two cases of ectopic pregnancy for diagnostic purposes. In the first case the x-ray picture clearly showed the ovum in the lumen of the tube. In the second case the picture revealed a uterine malformation and a high dislocated tube, the site of the ectopic pregnancy.

J. P. GREENHILL.

## Gynecology

Abad Colomer, L.: New Procedure for the Diagnosis of Ovarian Cyst, Rev. españ. obst. y ginec. 1: 287, 1944.

The author describes the sign discovered by Max Fourcstier to differentiate ascites from a cyst.

Paracentesis is performed 3 cm. from the umbilicus in the median line and, after evacuation of 2 c.c. of fluid, 200 c.c. of filtered air are injected through the puncture needle. In the case of a collection in a cystic membrane, the imprisoned air is shown on the film in semilunar form determined by the convexity of the swelling, while in ascites the air bubbles appear under the diaphragm separating it from the liver. The vertical position of the patient is essential in obtaining the picture.

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Mazza, Horacio L.: Recurrence of Genital Prolapse, Bol. Soc. de obst. y ginec. de Buenos Aires 23: 543, 1944.

The author reports four cases and, on the basis of previous experience and of the opinions expressed by other authors, draws the following conclusions.

Recurring prolapse is so frequent and sometimes constitutes such a serious disturbance that it deserves the greatest attention. Its cause lies in constitutional factors as well as in defects inherent in the operative process. Its surgical correction is perfectly feasible with the currently known techniques, provided that selective judgment is used which is also indispensable in prolapse in general. Although this is an atypical hernia, it is often necessary to adopt an eclectic criterion combining different procedures to obtain greater efficacy, which puts to the test the technical resources and the improvisation faculties of the surgeon.

J. P. GREENHILL.

Calvo Marcos, Miguel, and Botella Llusia, Jose: Condition of Ovaries in Cases of Uterine Myoma, Rev. españ. obst. y ginec. 1: 1, 1944.

The authors studied 91 cases and found that the gynecologist who claims normal behavior for the ovaries of myomatous patients and those who accept the constant presence of follicular cysts in those ovaries are both wrong. The truth lies in between the two claims.

The ovaries are frequently altered and only a small number of patients show evidence of a normal cycle. The latter occurs with relative frequency in women who develop myomas before the age of 40 years. The commonest type of ovaries is that with persistence of follicles and follicular cysts. This is more frequent in women nearing the menopause than in young women. Consequently, a certain relationship between the ovarian disturbances and the myoma may be accepted, but not an absolute correlation.

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Ercole, Ricardo: Urology in Gynecology, Bol. Soc. de obst. y ginec. de Buenos Aires 23: 570, 1944.

The author shows that in genital pathology of women trauma, inflammation, tumors, and even hormonal lesions have a repercussion on the urinary apparatus, sometimes producing lesions that are more serious than the genital lesion itself. In the study of gynecology

frequently causes menstrual abnormalities, amenorrhea, and dysmenorrhea. Hertzler found dysmenorrhea in 26 per cent of cases of toxic goiter. Schmitz recorded a high basal metabolic rate in 50 per cent of patients with dysmenorrhea. Meldolesi found menstrual disturbances in 76 per cent of cases of Basedow's disease, of which 25 per cent had amenorrhea; 53 per cent of the patients were at the age of puberty. Among endocrine factors causing sterility in the woman those of thyroid origin occupy a prominent place. Many of these cases are amenable to cure by surgical or medical treatment of the thyroid dysfunction.

Pregnancy imposes new metabolic requirements on the thyroid gland to which the latter responds in 70 to 80 per cent of cases, with hypertrophy and hyperplasia (work-hyperthyroidism) accompanied by increased blood content in iodine, increased iodine excretion through the urine, elevated basal metabolic rate and increased amount of thyroid hormone in the circulation. This functional hyperthyroidism explains the appearance of goiter during pregnancy in predisposed women in goiter-endemic areas and other cases in which a latent goiter becomes manifest during pregnancy. Regarding the relation of the thyroid gland to appearance of toxemia, the opinions are still controversial. According to Colvin and Bartholomew, young pregnant women with a basal metabolism over 10 per cent present little or no elevation of blood cholesterol and are apparently less predisposed to toxemia of pregnancy, while women with basal metabolism under 10 per cent have a hypercholesterolemia and are more likely to develop toxemia. The effect of dysthyreosis (hyper- or hypothyroidism) on the course of pregnancy is well known (abortion, premature birth, stillbirth, etc.). When a woman with hyperthyroidism arrives at term, the infant is normal in most cases, except in endemic areas where cases of congenital goiter are more common. The milk secretion is little affected by simple goiter, but may be disturbed in cases of thyrotoxicosis. Contrary to the contention of some, pregnancy does aggravate the course of pre-existing toxic goiter. The menopause produces new alterations in thyroid function, which in some cases may reach the proportions of hyperthyroidism, especially if simple or toxic goiter had been present before.

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### Extra-uterine Pregnancy

Delascio, D., and Assali, N. S.: Interstitial Ectopic Pregnancy, *An. brasil de ginec.* 18: 238, 1944.

The authors believe that the terms: "interstitial" and "intramural" pregnancy apply to the same pathologic process. Interstitial tubal pregnancy is extremely rare. The authors do not agree with those who claim that tubal endometriosis is the most important factor in the etiology of ectopic nidation of the ovum. Other factors, such as inflammatory processes, diverticula, etc., should be considered. The diagnosis of interstitial pregnancy is difficult. The presence of a hard, painful tumor in one of the uterine horns, its broad base at the uterus adjacent to the fundus, which produces asymmetry in the insertion of the tube as compared to the other side, and of a softer and larger uterus than in other ectopic pregnancies, suggest the possibility of interstitial pregnancy. To be considered in the differential diagnosis are: angular pregnancy; pregnancy in a rudimentary uterine horn; subserous myoma; subserous myoma with topical abortion; tubal isthmic pregnancy; and the Braun-Piskacek sign. The prognosis is serious owing to the marked vascularization of the uterine horn, and hemorrhage is much more profuse in interstitial pregnancy than in other tubal pregnancies.

Two cases of interstitial tubal pregnancies are presented. The first patient had a punctiform perforation on the posterosuperior surface of the left horn, covered with epiploon. The operation consisted of hysterectomy. The second patient had a large perforation of the right horn with irregular borders indicating a virtual "explosion" of the fundus. Because of the extremely poor condition of the patient, only resection of the horn could be performed. Despite blood transfusion, the patient died on the operating table.

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myomectomy scar, one case; villous penetration, one case; former molar gestation, one case; abdominal trauma, one case. In five cases the etiology could not be established. Among the cases which occurred during labor, the causes of rupture were: internal version (28.2 per cent); transverse presentation (15.3 per cent); forceps (15.3 per cent); scars (12.8 per cent); and fetal gigantism (5.1 per cent). The retention of the aftercoming head, contracted pelvis, Bandl's ring, and face presentation accounted for one case each. In four, no etiology could be found. In three cases the rupture occurred in the corpus (7.6 per cent); and in 36, in the lower uterine segment (92.3 per cent). There were 24 maternal deaths (61.5 per cent); 11 patients succumbed to hemorrhagic shock (28.2 per cent), 10 to generalized peritonitis (25.6 per cent), and one (2.5 per cent) to each of the following causes: endometritis with septicemia, myocarditis, and pelvic peritonitis. Fetal mortality was 76.9 per cent.

The treatment varied: subtotal or total hysterectomy, suture of the scar and expectancy. In recent years maternal mortality has been reduced thanks to the attention given to the general condition of the patient and to the methods to improve it, such as blood or plasma transfusion and administration of analgesic drugs which help the patient to endure the intervention. A still better prognosis is to be expected, at least for the mother, owing to the improved methods of treatment of obstetric and hemorrhagic shock and to the intra-peritoneal application of the sulfonamides.

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Otero, Francisco de Borja: Episiotomy. Technic to Obtain Anatomical Cicatrization, *An. d. Inst. matern. y asist. social, Buenos Aires* 5: 185, 1943.

Unlike the old methods which produce unsatisfactory cicatrization because of unequal retraction of the wound margins, the technique described by the author assures symmetrical approximation of the different layers.

Two Michel clamps are inserted on each side of the site of the episiotomy incision. After expulsion of the fetus, the clamps, although displaced together with the margins of the wound, indicate the position of the perineovaginal junction line. A catgut suture is passed through each of the clamps and lateral traction is exerted during the musculoaponeurotic suture, downward traction during the suturing of the vaginal incision and upward traction during suturing of the perineal skin. The technique is so simple that any physician can use it; the placing of the clamps can be done quickly and no anesthesia is necessary.

J. P. GREENHILL.

Morassi, A.: Medical Induction of Labor, *Obst. y ginec. latino-am.* 2: 867, 1944.

In 1931, Kreis advocated the following routine for women in labor: (1) artificial rupture of the membranes even if the cervix is dilated only 2 cm., and (2) the use of antispasmodics to overcome spasm of the cervix. By these measures, Kreis has been able to shorten considerably the duration of labor. This form of treatment is routinely carried out in Strasbourg. Morassi condemns this routine treatment of labor cases. He agrees with the Argentine School headed by Peralta Ramos who uses these measures only when indicated in cases of dysfunction of uterine activity in prolonged labor. In such cases obstetric and surgical interference is usually necessary in the interests of both the mother and the baby.

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### Miscellaneous

Copley, Alfred Lewin: Studies on Human Placental Thromboplastin, *Science* 101: 436, 1945.

In a short note, the author announces the production of high potency thromboplastin from the human placenta. Although the method is not given in this publication, it is stated that the thromboplastin is a protein phospholipid, fully as active as that produced

ecologic disorders, it is necessary to keep in mind the concept of pathology of the system in the anatomic and functional unit of the genitourinary tract. From this point of view, excretory urography is the method which provides the most important information on the condition of the urinary apparatus and should, therefore, be routine in the examination of the female genital tract. In cases in which this examination is insufficient, recourse must be taken to more specialized measures and the collaboration of the urologist should be useful.

J. P. GREENHILL.

### Gynecologic Operations

Gaston, Eugene A.: Total Abdominal Hysterectomy and the "Occasional Operator," Surg., Gynec. & Obstet. 80: 539, 1945.

In order to counteract the impression that total abdominal hysterectomy is an operation safe only in the hands of an expert pelvic surgeon, the author presents a series of 65 personally operated cases. He states that in a community of 25,000 persons there was an average of only 18.6 hysterectomies a year. Thus the general surgeon serving such a community could never become more than an occasional operator as far as this operation was concerned. The cases considered were all done for benign conditions and the total operation was performed in all instances unless contraindicated. The technique used was that described by Meigs, and adequate pre- and postoperative care was stressed. Using 35 supracervical hysterectomies as a control series, the author was unable to demonstrate any significant difference in mortality, morbidity, or postoperative changes in sex life. There was a slight increase in minor postoperative complications in the total group.

LT. L. M. HELLMAN, M.C., USNR.

Borras, Pablo E.: Strassmann's Operation in Some Uterine Malformations, Bol. Soc. de obst. y ginec. de Buenos Aires 23: 250, 1944.

The author states that in cases of separated double uteri it is not necessary to perform any surgical repair, while in cases of double uterus with one cervix or bicornuate uterus, repair is advisable. These malformations are usually found during a laparotomy or on the occasion of some complication. The author has always used Strassmann's operation which seems to be the most rational one.

The two uteri are located and the possibilities of repair are studied. The line of incision is traced along the internal border of each hemiuterus. After preliminary circulatory block, the cavity of each hemiuterus is entered along the line of incision, the cervical canal is located, and the internal orifice is adequately dilated. The two cavities are united and their posterior borders, fundus, and anterior borders are sutured. The operation is ended by reinforcing the suture of the walls with a layer of seromuscular peritonization.

J. P. GREENHILL.

### Labor: Management, Complications, Etc.

Frid, Isidoro J.: Fifty Cases of Rupture of the Uterus During Pregnancy and Labor, An. d. Inst. matern. y asist. social, Buenos Aires 5: 125, 1943.

Fifty cases of rupture of the uterus during pregnancy and labor are reviewed by the author. The present statistics are based on the material of the Institute of Maternity of the Alvear Hospital from 1912 to 1942. Among the 37,898 cases, including 31,173 deliveries, rupture of the uterus was found in 0.13 per cent of the cases. Hence, in a period of thirty-one years, there occurred 50 uterine ruptures. Eleven (22 per cent) occurred during pregnancy and 39 (78 per cent) occurred during labor. The maternal mortality among the cases which occurred during pregnancy was 45.45 per cent, and the fetal mortality was 81.81 per cent. The causes of the rupture were: scars from previous cesarean operation, two cases;

females to 151 males. The infant mortality showed a definite relationship with the age of the newborn, and was 52.9 per cent for the premature ones and 25.6 per cent for the children at term. The total mortality was 34.2 per cent.

The number of eclamptic attacks in the mother influenced notably the infant mortality, which was 29.1 per cent for mothers who had one to nine attacks, and 55.5 per cent for those with ten or more attacks.

Treatment by cesarean section gave an infant mortality of 11.4 per cent; by magnesium sulfate, 23.5 per cent; and by the Stroganoff Zweifel technique, 41 per cent. Nevertheless, the treatment with magnesium sulfate and hypertonic glucose solution is the treatment of choice which protects both maternal and fetal interests.

J. P. GREENHILL.

### Pregnancy: Complications, Etc.

Bidoire, A.: Acute Salpingitis and Pregnancy, *Gynéc. et obst.* 40: 519, 1939.

Acute salpingitis rarely complicates pregnancy because the two conditions are usually incompatible. The etiology of the salpingitis is either gonorrhea, puerperal infection or tuberculosis. The tubal involvement may precede the gestation, or it may begin with the onset of pregnancy. In the latter cases, the causative organism is either the gonococcus or the streptococcus. The complications which may arise are acute inflammation, pyosalpinx, and generalized peritonitis. The prognosis is bad. The diagnosis is difficult to make, but it is important because a decision must be made whether to treat the case medically or surgically. In the differential diagnosis the following must be considered: ectopic pregnancy, torsion of an ovarian cyst or suppuration of an ovarian cyst, and acute appendicitis.

Treatment is the same as if the patient were not pregnant. Whenever possible, it is best to wait until the fever subsides before operating. If a pyosalpinx is suspected, however, it must be removed.

J. P. GREENHILL.

Turenne, A.: Treatment of Intact Dead Retained Ovum, *Obst. y ginec. latino-am.* 3: 9, 1945.

The author advises a policy of expectancy when one diagnoses an intact, dead, retained ovum. Considering the element of uncertainty in such cases, the patients must be carefully examined from time to time, especially in the first six months when a definite diagnosis of fetal death is made. Treatment will depend on the duration of the pregnancy, the local and general condition of the patient, and the menstrual history (to avoid using oxytocics in the presence of genital hypofunction). It must be remembered that in some cases of fetal death during the last three months, there is a great tendency toward uterine atony and serious bleeding. The procedure chosen for emptying the uterus must carry the least risk for the mother, and it should preferably end in spontaneous evacuation of the uterus.

J. P. GREENHILL.

by Howell from pig lungs. In vitro it causes clotting of hemophilic blood intravenously in dogs; in small doses it shortens the coagulation time, the period of higher coagulability lasting up to two weeks. Used locally in dog surgery, it caused almost instantaneous coagulation of bleeding surfaces.

LT. L. M. HELLMAN, M.C., USNR.

Rodriguez de Ginocchio, Mercedes: Social Factors in Genital Hypoplasia, An. d. Inst. matern. y asist. social, Buenos Aires 5: 139, 1943.

The author states that aside from endogenous, constitutional factors, external factors play an important role in producing genital hypoplasia. The best known of these is the alimentary factor. The vitamin-hormone relationship, the effect of deficiency diseases on sexual development and function, on sterility, amenorrhea, tendency to abortion and prematurity, have been demonstrated clinically and experimentally. Social factors such as poverty, ignorance, fatigue, dietary regime, etc., are potent causes influencing the development of glands of internal and external secretion. Other important exogenous factors are infections, especially syphilis and tuberculosis because of their effect on the offspring and the changes they produce in the germ plasm. Malaria and ankylostomiasis may cause genital hypoplasia through the anemia they produce. Excessive sports or sedentary life, composition of the water, climate and the soil, are other factors which may influence the incidence of genital hypoplasia. Chronic intoxication, alcoholism, and morphine addiction are well known for their deleterious effect on the germinal elements and development of the ovum. Among the chronic intoxications apt to produce changes in the genital organs are industrial poisoning with arsenic, mercury, phosphorus, and benzol and its derivatives, lead and nicotine. Important factors in the configuration of the soft tissues of the body of the following generations are emigrations and successive racial intercrossings. The various opinions of the constitutionalist schools which aim to perfect the human race are reviewed.

J. P. GREENHILL.

### Newborn

Arnheim, Ernest E.: Congenital Ileal Atresia With Gangrene, Perforation, and Peritonitis in a Newborn Infant, Am. J. Dis. Child. 69: 108, 1945.

A case of congenital atresia of the ileum with gangrene, perforation, and peritonitis in a newborn infant is reported. This is the twelfth reported cure of atresia of the intestine below the duodenum and the second cure of a patient in this condition when perforation and peritonitis had supervened.

JAMES P. MARR.

Elizalde, P. I., and Latienda, R. I.: Prenatal Tuberculosis, Arch. Soc. argent. de anat. norm. y pat. 5: 576, 1943.

The authors have collected sixteen cases of prenatal tuberculosis which they consider authentic. In all of these cases, the infant was removed from the mother immediately after birth. Twelve of the cases probably had a hematogenous source, three were due to aspiration, and one had an intrapartum origin. The lungs were involved in all of the sixteen babies. The survival time of the infants varied from 24 to 245 days, with an average of 64 days.

J. P. GREENHILL.

Orengo Diaz del Castillo, F.: Study on the Newborn in Eclampsia, Rev. Españ. obst. y ginec. 1: 85, 1944.

The author found that, of 203 children born in Santa Cristina Maternity Hospital of Madrid of eclamptic mothers, 30.8 per cent were premature. The average weight of the children at term was 3,086 grams. The usual proportion of sexes was changed into 100

## Item

### **American Board of Obstetrics and Gynecology, Inc.**

The annual meeting of the Board was held in Chicago, Illinois, from May 5 to May 11, 1946, at which time one hundred forty-one candidates were certified.

A number of changes in Board regulations and requirements were put into effect. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. At this meeting the Board also ruled that it will not accept the nine months residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration, April 1, 1946.

The next written examination (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 7, 1947, at 2:00 P.M. Candidates in military service are requested to keep the Secretary's Office closely informed of changes in address.

Applications are now being received for the 1947 examinations. Closing dates for these applications will be Nov. 1, 1946.

For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

PAUL TITUS, M.D.

## Correspondence

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### Recurrent Placenta Previa

*To the Editor:*

Dr. Monrad E. Aaberg reports in the April, 1946, issue of this JOURNAL two cases of recurrent placenta previa and states that a review of the literature reveals only 10 instances of recurrent placenta previa in successive pregnancies. He has overlooked the case reported by us, C. J. Andrews and Richard B. Nicholls, in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 42: 538, 1942. Also, the case of J. Binder, in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY 28: 92, 1934. Our patient had placenta previa in three successive pregnancies.

This information does not change the conclusion of Dr. Aaberg, that recurrent placenta previa is an uncommon obstetric complication, but it is obviously desirable that the record should be as accurate as possible.

C. J. ANDREWS, M.D.

RICHARD B. NICHOLLS, M.D.

NORFOLK, VA.

MAY 24, 1946.

### Traveling in Pregnancy

*To the Editor:*

It has been a time-honored custom to interdict traveling during pregnancy. Yet, the taking of a journey, either long or short, is sometimes necessary under such circumstances because of the economic dependence of the wife on her husband, as well as her desire to be near him. Mary and Joseph made a long noneconomical journey near term without mishap, and when a stillbirth would have affected the destiny of the entire world.

During World War II, travel by pregnant women on land, sea, and in the air, by train, automobile, boat, and plane, took place on an unprecedented scale. Yet general practitioners and obstetricians alike, whether in private practice or in the military service, have not observed any untoward effects; the normal hazards of travel not included.

This vast experience, as well as scattered reports on the subject, has not disclosed any increase in the incidence of miscarriage, premature labor, placenta previa, or toxemia. Moreover, the lowering of the maternal and infantile mortality rates throughout the nation bespeaks the relative innocuity of commodious travel per se.

Yet, physicians are known to refuse permission for their patients to travel, going so far as to refuse to discuss the matter. The doctor who is called upon for prenatal care, knowing that the patient will leave his jurisdiction after several weeks or months can render great service to the patient and to his contemporaries if he would proceed with prenatal care as if he were going to perform the delivery. The payment of prorated fees to cover each visit, laboratory tests, and a complete transcription of the record can be expected of most patients, including those participating in the EMIC program. Much delay and writing back and forth is avoided if the patient carries the record with her.

It may be fitting for the Committee on Maternal and Infant Care to study various prenatal forms now in use and consolidate them into one standard form for use by physicians on a national scale, as a distinct contribution toward improvement of maternal care in general, and also of the many women who will continue to travel during pregnancy.

CARL T. JAVERT, Lt. Colonel, M.C.

A.A.F. STATION HOSPITAL

RIVERSIDE, CALIF.

MAY 2, 1946.



TABLE I. FETAL MORTALITY IN BREACH DELIVERY

HOSPITAL	AUTHOR	YEAR	WEIGHT (GM.)	STILLBIRTH AND NEONATAL MORTALITY—PER CENT					
				TOTAL			PRIMIPARA		
				NO.	GROSS	COR- RECTED	NO.	GROSS	COR- RECTED
Eight British Maternities	Gibberd	1931		218	52.0		269	32.0	
Guy's Hospital	Gibberd	1931		55	34.0		204	29.0	
Royal Maternity, Belfast	Macafee	1937		118	23.7	10.0	231	39.0	3.4
Liverpool Maternity	Burns	1941	2,250+	286	6.2		176	5.5	
Glasgow Royal Maternity	Annual Report	1938-43							
Simpson Maternity, Edinburgh	Annual Report	1943 & 44		105	6.6		62	6.4	
Boston Lying-in Hospital	Goethals	1940	2,500+	200	9.9		200	5.0	
New York Lying-In Hospi- tal	Marchetti	1943	1,500+		13.1	3.5		14.8	
Philadelphia Lying-In Hos- pital	Mohler	1938	all	709	26.0	5.5	295	22.7	7.3
Philadelphia Lying-In Hos- pital	Tompkins	1943	1,000+	211	10.4*	2.7†			
Sloanes Hospital	Watson	1943			5.3				
Margaret Hague	Waters	1942	2,500+	675	11.2		404	12.3	
			Premature	184	46.7				
St. Louis Maternity	Soule	1936	2,500+	296	9.1	7.5			
Cleveland Maternity	Cannell and Dodek	1934	1,500+	562	19.2				
			2,500+	400	8.5	6.8			
University of Maryland	Siegel and Me- nally	1939		167	28.1	12.1			7.0
Brooklyn, N. Y.	Gordon, et al.	1934	400+	3301	20.3	15.3			
			2,500+	2557	16.7	12.6			
			400-2,499	302	70.0		849	6.7	
Chicago Lying-in Hospital		1941-45	400+	662	11.9				
			2,500+	524	3.8	1.7			

\*All deliveries by 17 certified obstetricians.

†1,500+ Gm. and corrected.

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## Original Communications

### FETAL MORTALITY IN BREECH DELIVERY

WILLIAM J. DIECKMANN, M.D., CHICAGO, ILL.

*(From the Department of Obstetrics and Gynecology, University of Chicago, and  
the Chicago Lying-in Hospital)*

**B**REECH delivery, according to reports, still has a mortality ranging from 3.8 to 52 per cent. The average gross mortality is 7.7 per cent, corrected to 4.2 per cent, for term fetuses on five maternity services. External cephalic version in all cases, and elective cesarean section in primiparous patients at term where version fails, have been suggested procedures to decrease the mortality.

A study of the reports on breech delivery for the past fifteen years indicates that obstetricians still have many different ideas about the conduct of the delivery. What is most important is that little has been done to reconcile conflicting statements, to evaluate the causes of this high fetal mortality, and to institute measures to lower it. Some clinics have lowered their fetal mortality by an evaluation of each case early in labor, based on a systematic treatment for all breech presentations. I have believed for many years that the best clinical test of a doctor's obstetric ability is his management and delivery of a breech presentation.

We divide breech presentations into single (frank), legs extended and thighs flexed; and double (full, complete, foot, knee), legs and thighs flexed. We believe that the single or double footling, knee, etc., are all modifications of the double breech, and the presence of one or both feet make traction possible at any time, thus differing from the single type where the "breaking up" of the breech becomes very difficult and at times impossible, due to the failure of the uterus to relax under deep anesthesia. Several writers have suggested that the splinting of the fetal body in a single breech prevents engagement and lateral flexion during delivery (the latter retarding descent), and also makes external cephalic version difficult. In a patient with a normal pelvis, the double breech

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NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

cent in multiparas were due to intraeranian hemorrhage. They do not practice external cephalic version. They state "it is our practice to frequently elect cesarean section in breech cases, particularly in primiparas." Eighty-five sections, 10.8 per cent, were performed. Breech delivery is effected under deep anesthesia by obtaining both feet and extracting slowly, "after making sure that the *lower uterine segment is effaced* and the *external os completely dilated*." The head is pushed through the inlet in the transverse, then rotated, and the Piper forceps applied if necessary.

M. Potter states that, although he has had considerable experience with the extraction of arms and aftercoming head, he considers breech delivery as one of the most serious complications in obstetrics.

Walsh and Kuder reported a fetal mortality of 12.5 per cent (breech mortality for all patients was 13.1 per cent) for breech delivery in elderly primiparas at the New York Hospital. Twenty-nine per cent of the deliveries were by cesarean section, although the clinic incidence of section is 2.3 per cent. Their total maternal mortality is 0.198 per cent, but it was 3.6 per cent in this group of breeches. They advocate a careful evaluation of all breech presentations and the use of cesarean section if any complications similar to our listing are present.

Bill, discussing Potter's report, states that the arms become extended if the lower uterine segment is tight. In several discussions he emphasizes the value of *complete dilatation and deep surgical anesthesia*.

The corrected fetal and neonatal mortality of 2.7 per cent reported by Tompkins in Table I for breech deliveries, either conducted or supervised by seventeen diplomates of the American Board, indicates the importance of experience. I am certain, however, that these same obstetricians have a much lower corrected mortality for vertex presentations.

TABLE III. BREECH DELIVERIES IN HOSPITALS OF BROOKLYN, N. Y., 1926-1930

WEIGHT 2,500+ GM.	SPON- TANEOUS AND ASSISTED	EXTRAC- TION	BROKEN UP	TOTAL	CESAREAN SECTION
Number	1597	555	405	2557	44
Fetal mortality—per cent					
Total	6.7	18.7	28.9	16.7	0.45
Primipara		20.9	28.0		
Multipara		16.7	30.0		
4000+ Gm. primipara	6.1	19.2	25.4		
4000+ Gm. multipara	3.6	16.0	31.0		
Fetuses injured	2.0	5.0	9.9	3.9	0

Twenty-one maternal deaths—5 from causes not directly associated with labor. In the other 16 cases, death was from rupture of the uterus (3), pulmonary collapse (1), hemorrhage and shock (4), and septicemia (8). A total corrected mortality of 0.49. Five of the 16 deaths occurred in the 44 cesarean sections, 11.4 per cent maternal mortality. (*Am. J. Obst. & Gynec.* 28: 140, 1934. C. Gordon, R. Garlick, and P. Oginsz.)

The data in Table III depict the fetal and maternal mortality associated with breech delivery in a large city. It is obvious that parity of the patient, size of the fetus, and abnormalities of labor were the important factors in producing mortality. These figures are old, but in view of the continued high fetal mortality reported in many hospitals, they are, in all probability, still valid. In 1942 there were 2,356 breech deliveries in Chicago. Twenty-four per cent required varying degrees of interference. The fetal mortality figures are not available, but are undoubtedly high.

is more likely to engage than the single; but less likely than a vertex presentation. The difficulty in single breech in performing external version and in obtaining the feet in "breaking up" indicate the tightness of the uterus. The significance of single breech in vaginal delivery is evidenced by the fact that 85 per cent of our term and 70 per cent of our premature (1,500 Gm.) stillbirth and neonatal deaths were single breeches. The deaths due to delivery, excluding macerated fetuses and those due to major malformations and neonatal disease, were single breeches in 67 per cent of the premature and 100 per cent of the term babies. Cannell and Dodek reported that 79 per cent of the term fatalities were single breeches. Single breech was also of greater significance in primiparas, in that 67 per cent of the corrected term and 60 per cent of the premature deaths were single breeches.

Table I lists data from several maternity services as illustrative of the variations and magnitude of fetal mortality in breech delivery. The mortality is still high, even after it is corrected by deleting stillbirths, anomalies, and neonatal deaths which could not be attributed to the delivery.

Gibberd, in 1931, reported an analysis of breech deliveries as published in the annual reports of eight of the leading maternity services in Great Britain. He noted that in 269 uncomplicated breech presentations, the total fetal mortality was 29 per cent, and in the complicated cases (breech labor in a primipara) it was 52 per cent. For comparison, he gave the figures at Guy's Hospital, included in the above figures, but reserved the term "complicated breech" for cases in which some additional abnormality, such as placenta previa or prolapsed cord was present. The mortality in uncomplicated breech in primiparas was 30 per cent, and in multiparas 22 per cent, while in complicated breech it was 71 per cent in primiparas and 58 per cent in multiparas. When the figures were corrected for macerated babies, etc., he found that there was a fetal mortality of not less than 28 per cent in primiparas and 15 per cent in multiparas.

Goethals at the Boston Lying-in Hospital has made the most extensive study of a large number of breech deliveries over a period of years, and his papers should be read by every obstetrician. Goethals advocates extraction at full dilatation. The excellent results from the Boston Lying-in Hospital are given in Table II. He states that 7 per cent of their primiparous breeches were de-

TABLE II. FETAL MORTALITY IN BREECH DELIVERY (GOETHALS)

TERM FETUSES	1913-20	1921-28	1928-37	CESAREAN SECTION
Primiparas	9.8%	9.0%	5.0%	3.1% (32 deliveries)
Multiparas	13.0%	7.0%	4.5%	10.0% (20 deliveries)

livered by cesarean section. Breech presentation, per se, on their service offers a tenfold risk as compared with vertex, 6.9 per cent against 0.7 per cent. E. Potter stated that the mortality for infants and fetuses of 400+ Gm., exclusive of those who were dead before the onset of labor, were malformed or had erythroblastosis; on our service for the period 1931 to 1940 inclusive was 9.3 per cent for breech against 1.1 per cent for cephalic, and for 1941 to 1942 inclusive for infants and fetuses of 1,500+ Gm. (corrected in the same manner), were 3.0 per cent against 0.68 per cent.

M. Potter, Erving, and Brown recently reported 786 breech deliveries with an uncorrected fetal mortality of 19.2 per cent, and a corrected one of 9.6 per cent. The corrected mortality in primiparas was 9.6 per cent, and in multiparas, 8.1 per cent. Seventy-five per cent of their fetal deaths in primiparas and 34 per

times after the completion of the version. The latter must be stopped or reversed if there are any marked irregularities in the heart rate. If difficulty is encountered, an x-ray picture should be obtained. Anesthesia should not be used and no undue force should be exerted.

TABLE IV. BREECH DELIVERIES, 1941-1945

WEIGHT (GM.)	NUMBER	STILLBIRTH AND NEONATAL MORTALITY (PER CENT)
400- 999	24	100.0
1,000-1,499	34	39.2
1,500-2,499	80	26.2
400+	662	11.9
1,000+	638	8.6
1,500+	604	6.8
2,500+	524	3.8
Alive at onset of labor		
1,500+	604	4.8
2,500+	524	3.1
Excluding antepartum deaths, fetal anomalies and diseases, and maternal complications		
1,500-2,499	80	11.1
1,500+	604	3.0
2,500+	524	1.7

Table IV gives the data for the last four years on our service. Our incidence of breech was 6.7 per cent for fetuses weighing over 400 Gm., and 4.6 per cent for those weighing over 1,000 Gm. Twin babies weighing 2,500 Gm. or more are included. One should consider only those babies weighing between 1,500 and 2,499 Gm., and especially those weighing over 2,500 Gm. It is apparent that whether one considers the mortalities for the groups where the baby was alive at the onset of the delivery, or where the doctor was presumably responsible for the death, our mortality in breech deliveries has been extremely low compared with previously reported figures. The senior obstetrician is in charge of the service, but this does not imply that he is present at every breech delivery. Many of the deliveries are under the supervision of the resident. However, the latter has had a minimum of two or more years of training before he is given this responsibility. The patients have been screened for contracted pelvis, for other major complications, and are usually seen by the senior or junior obstetrician while they are in labor, where further screening is carried out. Any abnormalities of labor demand consultation. There are no deletions. The 524 babies weighing over 2,500 Gm., and the 80 premature comprise the entire number of babies born by breech between July 1, 1941, and July 1, 1945. The mortality should even be less than this because several babies were lost as a result of inexperience or errors in judgment on the part of the resident and attending obstetricians.

Breech deliveries (1,500+ Gm.) comprised 4.4 per cent of our deliveries, but the breech mortality was 10 per cent of the total fetal and neonatal deaths; 13 per cent of the premature, and 6 per cent of the term.

The causes of death in our hospital associated with breech delivery have been prematurity, intracranial injury, and asphyxia because of inability to deliver head (rarely because of disproportion, and usually because of an incom-

*External Cephalic Version.*—Twenty to forty per cent of the fetuses present as breech some time between twenty-eight to thirty-six weeks; but the incidence of breech at term is only 4 to 5 per cent. It is difficult to decide which baby will not turn and also, if the external version is successful, how to keep the fetus from reverting to its former position. The objections to version are the risk of placental separation, of fetal asphyxia, and of abnormal presentation. Strangely, several advocates of version warn against its use in single breech because of the many failures due to the extended legs; and of the possibility of producing a compound presentation (McCulloch). Various specialists, discussing Ryder's article on external version, give an excellent review. Since 70 to 90 per cent (82 per cent in our service) of the breech presentations are single, the feasibility and advisability for cephalic version are limited.

Marchetti pointed out that the incidence of breech delivery at the Sloane Hospital where they perform external version is 3.8 per cent, as compared with 4.5 per cent at the New York Hospital where it is not practiced. Newell, at the Boston Lying-in Hospital, reported 1,160 attempted external versions in 784 breech presentations, beginning at twenty-eight weeks and on to term. Seventy-two per cent were successful. Routine repeated external version reduced the incidence of breech delivery from 3.8 to 2.3 per cent. The gross fetal mortality was 4.0 per cent, a reduction, according to Newell, of 38 per cent. Spontaneous version occurred in 19 per cent of the cases.

Siegel and McNally collected 1,749 cases of attempted version and found that there were 1,485, or 84 per cent, in which it was successful. In a total of 2,269 external versions, the fetal mortality was 3.3 per cent. They were successful in their own 68 cases in turning 81 per cent, with a gross fetal mortality of 1.8 per cent.

Moir reports that external version is successful in 76 per cent of primiparas and 97 per cent of multiparas. He states that if external version fails in a 40-year-old or older primipara, she should be offered a cesarean section.

Ryder reported that breech presentations were found in 258 cases out of 1,700 private patients, and that external version was successful in all but 54, 18 per cent. The fetal mortality in the 258 babies was 3.1 per cent, but that due to dystocia from breech delivery, was 0.8 per cent. However, only 54 were breech presentations at delivery, and 21 of these were delivered by cesarean section. Therefore, the mortality is 3.7 per cent; corrected, 6.0 per cent (2 in 33).

Believing that breech delivery is a major procedure that can only be learned by practice, I have never urged external version because the cases are needed for teaching. A cephalic position is of paramount importance when a test of labor is planned in borderline pelvis.

### Method

The patient's bladder and rectum must be empty. The abdomen should be well powdered. If the Trendelenberg position does not free the breech, the latter must be pushed up by rectal or vaginal finger. The breech is moved first to the side of the small parts, thus favoring flexion, and then pressure is used on the head. Rarely, the version is easier in the opposite direction. The version should be done slowly and gently, taking ten or more minutes to turn the fetus. The fetal heart beat must be obtained before, frequently during, and several

one to four previous breech deliveries terminating in stillbirths or damaged babies. Elective cesarean sections were performed for the present breech presentations. The other indications were repeat section, contracted pelvis, placenta previa, or toxemia.

Local anesthesia was used in the spontaneous delivery of single breeches in 50 per cent of the primiparas and 20 per cent of the multiparas. It was rarely used in double breech.

Forceps to the aftercoming head were used in 81 per cent of the extractions in primiparas, and in 70 per cent of the multiparas.

There were two maternal deaths in this group. A cesarean section was performed at 32 weeks' gestation because of severe pre-eclampsia in a primipara. The patient died from pulmonary embolism on the thirtieth postoperative day. A primipara with heart disease and pre-eclampsia delivered twins (second was breech) at 33 weeks, decompensated during labor, and died forty hours after delivery.

A breech presentation should always suggest some abnormality of: fetus, pelvis, or uterus (congenital malformation or tumors). In a primipara it should suggest a contracted pelvis or disproportion because of a large fetus.

Prolapse of the umbilical cord before complete dilatation is a serious complication. Goethals reported an incidence of 3.4 per cent, which was seven times that occurring in cephalic presentations.

*Bag.*—An intrauterine bag may be inserted either to stimulate contractions and/or to force cervical dilatation. There is no unanimity as to the size of the bag. We select a bag as large as the fetal head and preferably use no traction for at least twelve hours. The forceable extraction of the bag prevents the taking up of the cervix into the lower uterine segment, thus leaving a large cuff of cervix which will cause difficulty in delivering the head.

I prefer a 9 to 11 cm. Voorhees' bag, depending upon the size of the fetal head, inserted into the vagina (so far as I know, first suggested by DeLee) in all patients with double breech to prevent prolapse of the cord or of the feet, to stimulate uterine contraction, and to dilate the vagina. I also use the vaginal bag in all single breeches for its stimulation of contraction, and also for its dilation of the vagina. The latter makes the delivery of the shoulders and the head easier, and lessens the extensive lacerations in the upper vagina that so frequently occur. If the labor is progressing rapidly, the bag will soon be descending with each contraction, and it can be collapsed and removed. It may be left in place for twenty-four hours or longer. Vaginal bags were used in approximately 10 per cent of the primiparas and 3 per cent of the multiparas. A more extensive use of bags would have resulted, in all probability, in a lower fetal mortality.

*Treatment.*—After 32 weeks, an external cephalic version should be attempted and repeated at weekly intervals if the breech presentation recurs.

The patient with a breech presentation after 35 weeks' gestation in early labor or with ruptured membranes should have a careful examination and evaluation of the following: reproductive history, age, parity, pelvis, and size of

pletely dilated cervix). Potter and Adair stated that in the 1,050 breech deliveries (400+ Gm.) from 1931 to 1940, intracranial hemorrhage was found in 43 per cent (81 per cent had autopsies). Intracranial injury, in autopsies, has been well studied by Holland. Ford and Crothers, and Benda have reported studies on those babies who live after birth trauma.

Twenty-three per cent of the prematures were found to have no demonstrable cause for death at autopsy. A careful study of these patients' charts show that while analgesic drugs were used infrequently, yet anesthetics were used at delivery. Just what part analgesic drugs and anesthesia at delivery played in the failure of these premature babies to survive is difficult to say. I believe that women in premature labor should have no analgesic drugs and should have a minimal amount of anesthesia at the delivery, the latter if possible being conducted under local anesthesia.

The fetal mortality, even after correction, is greatest in the prematures and abnormally large babies. It is so high in the premature that Kellogg suggested abdominal hysterotomy as the treatment. Unfortunately, according to E. Potter, edema of the meninges occurs most frequently in prematures delivered by section. The omission of sedative drugs, the use of local anesthesia, and the ability to recognize a completely dilatable cervix will result in a marked decrease in the mortality of premature babies.

The high fetal mortality in babies weighing 4,000 Gm. or more, especially in primiparas, is difficult to lower, even though the obstetrician is experienced. External version usually fails in these cases because of the tight uterus and abdominal wall. Intrauterine fetal measurements and estimates of fetal weight are notoriously unreliable. Certainly every attempt should be made to evaluate fetal and pelvic size, and the character and course of the labor early enough to permit the performance of a safe cesarean section.

Major congenital anomalies are present in 0.57 per cent of our reportable fetuses. The incidence in our fatal breech deliveries was 1.8 per cent. Gordon and his associates report an incidence of 2.3 per cent for the breech deliveries in Brooklyn. Cannell and Dodek report an incidence of 2.7 per cent on their service. This increased incidence of abnormalities does not justify the sacrifice of any fetus just because it presents as a breech.

There were thirteen fractures of the humerus, clavicle, femur, or skull bones; one rupture of the liver, over seven intracranial injuries, and five craniotomies. Our incidence of fetal injury was 2.1 per cent. Cannell and Dodek reported an incidence of 1.6 per cent; Gordon and his co-workers, 3.9 per cent; and Gibberd, 5 per cent. The increasing incidence of injury as the delivery becomes more difficult is shown in Table III. Deep anesthesia, experience, and lack of haste will decrease the possibility of injury.

There were 67 cesarean sections (10.5 per cent for fetuses of 1,000 Gm.) with two neonatal deaths; a 1,550 Gm. fetus from a mother with a placenta previa, and a 1,240 Gm. fetus in a toxemic patient. Cesarean section in patients with normal pelvis was performed in 13 cases because of maternal age, size of the fetus, postmaturity, or previous stillbirth. Several patients had had from



Over 80 per cent of the breeches are single (frank) breech. We do not believe in a routine prophylactic "breaking up" of the breech and pulling down one or two legs, but do use this procedure in selected patients where labor is unduly slow. There is too much danger of prolapse of the cord or feet. However, the patient should not be permitted to labor until the breech is impacted in the pelvis and then cannot be broken up. Naturally, if the breech, either single or double, descends rapidly, the patient should be prepared for delivery as soon as there is crowning.

The experienced obstetrician who has examined many patients vaginally knows that the cervix remains completely dilated in the primipara only as long as something is holding it open, be it the head, breech, or bag. In the multipara, the completely dilatable cervix can always be palpated except momentarily as the presenting part is coming through it. What is of importance is that the doctor must be able to recognize a *completely dilatable* cervix with the presenting part at the inlet, as will be found in many patients with breech, floating head, or with a transverse presentation. In these patients, if the operator has any experience—and the inexperienced doctor should obtain consultation, he is not competent to deliver this type of breech—the patient should be surgically anesthetized with drop ether, which requires ten to twenty minutes if the mask is surrounded by wet towels. Chloroform or drop ether are the only anesthetics that will completely relax the uterus when it is necessary to "break up" a breech. Complete relaxation of the uterus cannot be obtained with any of the gas anesthetics. If no skilled anesthetist is at hand, the doctor can scrub and don gown and gloves, anesthetize the patient with ether, and then change gloves and gown, leaving the anesthesia to someone else and complete the delivery.

Willson, on our service, states that the pelvic floor is relaxed to a greater degree under spinal anesthesia (40 to 50 mg. novocaine) than under general anesthesia. We plan to try curare (intocostrin) for its relaxing effect on the recti and levator ani muscles.

The vagina should be well lubricated with thick soap if a vaginal bag was used, and manually ironed out if one was not used. Both feet should be obtained, and slow downward traction made. Usually Pinard's maneuver fails because of the tight uterus, and the doctor has to grasp the feet and pull them down. When the feet are through the vulva, a deep episiotomy should be performed. The delivery should be *slow*, with traction in the proper plane (posterior). Anesthesia can be stopped when the umbilicus is visible. In many patients the shoulders can be delivered as they present, but in a difficult case one must gently and slowly rotate the body of the baby back and forth with slight traction until one or the other scapula appears under the symphysis. The fingers can then be hooked in the elbow, or the humerus can be splinted and the arm wiped over the baby's chest and delivered, and the other shoulder rotated anteriorly and delivered (Potter). Rarely, one has to pull the posterior shoulder into the pelvis and then rotate it anteriorly. I doubt if a nuchal arm ever occurs.

the fetus (determined by McDonald, Ahlfeld, or comparable measurements). An x-ray of the fetus and pelvis may be indicated. Delivery should be by an elective cesarean section if the pelvis is (1) contracted, or (2) borderline with a large baby. Occasionally the operation is indicated if the fetus is of unusual value because, if the head sticks, the baby is either stillborn, or would have been better stillborn than living with intracranial injury. Primiparas who are 35 years and older with large babies (4,000 Gm.), unless labor progresses normally, should have a cesarean section.

The final decision as to the management should be made after six to eighteen hours of labor and/or ruptured membranes. The obstetrician should consider (1) vaginal delivery (use of vaginal or intrauterine bag or "breaking up" of single breech if labor is slow), or (2) cesarean section (faulty uterine mechanism).

The contractions are weak and the intervals long in many breech labors. Large doses of analgesic drugs should not be used unless the labor is normal (contractions lasting 40 to 50 seconds at 2 to 3 minute intervals, and cervical dilatation progressing normally as determined by vaginal examination). One dose of 0.2 to 0.4 Gm. sodium amytal, followed by nitrous oxide or ethylene anesthesia may be used.

In the test of labor in a breech, one is guided primarily by the length of time it takes for the cervix to dilate. If the cervix dilates completely, the doctor must decide whether or not the head can be delivered vaginally. In most pelves, 4,500 Gm. babies can be delivered as a breech if the obstetrician is skilled. The obstetrician with average experience should perform cesarean section for breech fetuses weighing over 4,500 Gm. If contractions are faulty and dilatation is slow, and if there are any complicating factors, such as previous stillbirths, age, or sterility, a cesarean section should be considered. Patients come to an obstetrician in order that they may survive and be in good health and, at the same time, have a healthy baby. In general, where the obstetrician begins with a live baby but delivers a dead or badly injured baby, or by craniotomy, he has performed poor obstetrics.

The question of spontaneous delivery of the breech, of manual aid, of breech extraction by "breaking up" or "decomposition," or the latter after a period of one or two hours, is an academic one. Difficulties in the delivery of breech are in achieving and recognizing a completely dilatable cervix, and delivering the shoulders and head. If the doctor is experienced in the management of aftercoming shoulders and head, a breech extraction should be no trouble for him. It is worth while to practice elective internal podalic version in suitable cases in order that one gain this necessary experience in the management of the aftercoming shoulders and head. We select multiparas with intact membranes, a completely dilatable cervix, and a high head for teaching elective podalic version. This is at variance with M. Potter, who states that any comparison between elective podalic version, which he practices, and breech delivery is untenable "because in a breech delivery it is impossible to control the arms, the head is always unmolded and is frequently extended. In an elective internal podalic version these three uncontrollable complications can be avoided."

If the breech does not engage with 9 to 10 cm. dilatation, and if, after one or two hours' time, there has been no change in the dilatability of the cervix, a Dührssen incision may be made at 6 o'clock and the breech broken up and extracted. It is difficult and usually impossible to make the incision if one waits until shoulder or head dystocia occurs. Our practice is to bring down only one foot if there is any question about the dilatability of the cervix, because the buttocks and one thigh are larger than the former alone.

When the breech crowns, and especially if it is a single breech, the perineum is infiltrated with 0.5 per cent novocaine, an episiotomy performed, and as soon as the breech is stemmed under the symphysis, the patient is anesthetized with drop ether and the remainder of the delivery is completed by the physician.

In a double breech, as soon as the cervix is completely dilatable, either with the feet presenting at the introitus or still within the vagina, the delivery is completed. Nothing is gained by delay.

After delivery, the vagina, cervix, and lower uterine segment should be palpated and inspected for lacerations and ruptures from the shoulders or after-coming head.

The breech in which dilatation and descent occurs normally gives little trouble, and the fetal and neonatal mortality will be low. Admonitions such as "hands off," "masterly inactivity," without instructions how to detect and to correct abnormalities in labor are dangerous. The indications for interference given by Sherman—maternal distress, impacted breech, tonic uterus, no advance with full dilatation for three hours, no advance into inlet in slightly contracted pelvis—will not save many babies' lives and will result in an increased maternal mortality. When these conditions are present, the doctor has waited too long.

The following cases are examples of poor obstetrical judgment:

A 38-year-old gravida v, para iv, 31 weeks' gestation, in labor 74 hours. A 5 cm., and later a 9 cm. intrauterine bag were used. Extraction of a 1,580 Gm. fetus with rupture of the uterus, incomplete hysterectomy, and blood transfusions. Survival of the mother, but death of the fetus from intracranial injury.

A 36-year-old gravida ii, para 0, was treated for mild toxemia during pregnancy and, on August 1, at 43 weeks' gestation, the membranes ruptured. On admission, the cervix was 5 cm. dilated and thin. During 118 hours of intermittent labor, the patient had eight rectal, but no vaginal examination. The blood pressure and proteinuria increased. Several notes by the attending obstetrician were "watch" and "continue careful observation." Finally on August 5, at 10:20 p.m., the fetal heart could not be heard, the breech was with great difficulty broken up (contraction ring) and a 3,940 Gm. stillborn baby was delivered. A vaginal examination within the first twenty-four hours might have revealed a completely dilatable cervix or an uneffaced cervix. If the latter were found, a cesarean section should have been considered within the first twenty-four hours (primiparity, age, postmaturity, toxemia, and abnormal labor).

### Conclusions

Breech delivery has a gross mortality of 7.7 per cent, corrected to 4.2 per cent for term fetuses on maternity services. The mortality in prematures is over 25 per cent.

The breech deaths are due to prematurity, intracranial injury, asphyxia, and a small number of visceral injuries.

With the patient surgically anesthetized with drop ether, there is no resistance from the pelvic floor or from the abdominal muscles. The baby should straddle the forearm, one or two fingers of one hand are inserted into the baby's mouth, producing flexion of the head, and gentle pressure exerted from above until one can determine in which diameter the baby's head will best enter the pelvis. This may be in the anteroposterior, oblique, or in the transverse. Forceps should never be applied to the head at the pelvic inlet. This is what causes intracranial injury. Once the head is in the pelvis, the doctor can in most cases deliver it by increasing flexion and pressure from above. Where this fails, forceps should be applied early, and the delivery should be by the "combined method." If there is any delay, the posterior perineum must be retracted and the blood wiped out, thereby exposing the baby's mouth and permitting the baby to breathe. None of the forceps, even the Piper, are constructed so that they will cause flexion of the aftercoming head. This is of the utmost importance. In the "combined" maneuver (see Fig. 1) forceps are applied by one operator, the other with the baby straddling his forearm, pushes from above, and at the same time flexes the baby's head with his fingers in its mouth. One will be amazed at the ease with which babies' heads can be delivered.

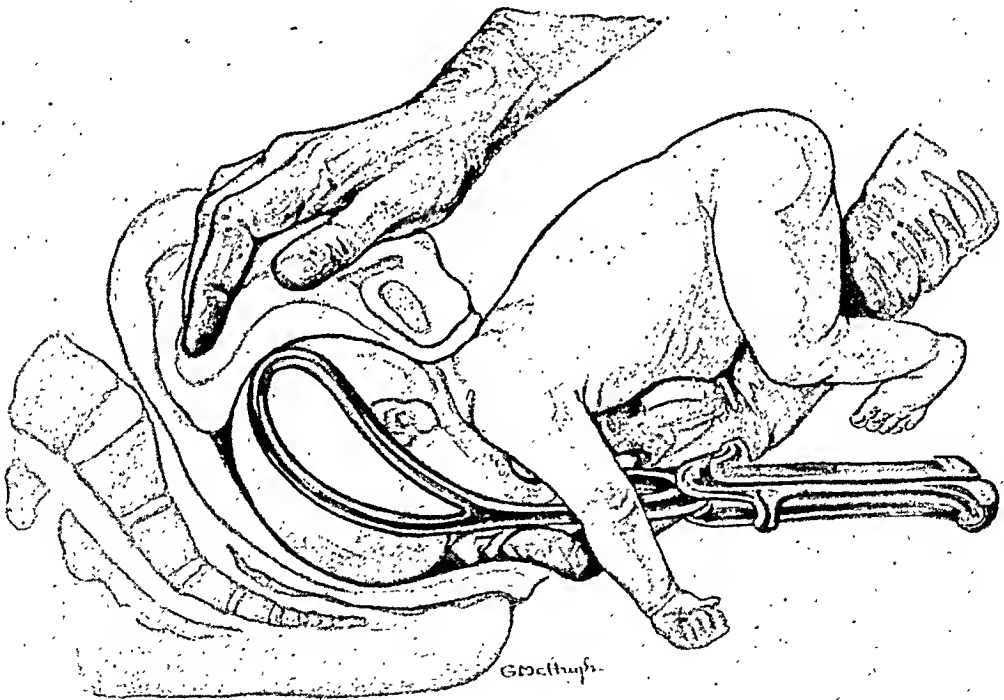


Fig. 1.—Illustration showing the application of the forceps combined with the Celsus-Wiegand-Martin maneuver for delivery of the aftercoming head after it is through the inlet.

We do not approve the Mauriceau-Smellie-Veit or Prague maneuvers because of the real possibility of intracranial hemorrhage. The Celsus-Wiegand-Martin maneuver (flexing head and pressing suprapubically), especially if the patient is surgically anesthetized, is effective in most cases in delivering the head. Where it fails, forceps should be used as described under the term "combined."

# THE FETAL RISK IN BREECH DELIVERY

## A Study Based on 708 Cases

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STATISTICS from many clinics over a long period of time have shown a high fetal mortality rate in breech as compared to vertex delivery. Despite refinements of technique, there has been no significant improvement since Holland,<sup>1</sup> in 1922, showed that 75 per cent of the term fetal deaths in breech deliveries are due to laceration of the tentorium cerebelli with subdural hemorrhage.

There is, furthermore, no agreement as to the amount of fetal risk involved in breech delivery itself. This is in part due to the fact that no standard has been generally accepted for the exclusion of complicating factors, and, as a result, the corrected fetal mortality rates of different authors vary considerably.

The wide variation in the results reported from several clinics is shown in Table I. These differences are mainly due to the disagreement as to what constitutes a normal, uncomplicated breech delivery. As examples, Moore and Steptoe<sup>2</sup> include infants weighing 1,500 Gm. or over in their figures; Caldwell and Studdiford<sup>3</sup> include infants weighing over 4 pounds (1,800 Gm.); Hawker and Soule<sup>4</sup> include only infants weighing over 2,500 grams. Likewise, in correcting for cases which might add to the normal risk of breech delivery, Goethals,<sup>5</sup> and Macafee and McClure<sup>6</sup> eliminate cases of cord prolapse; Moore and Steptoe,<sup>2</sup> on the other hand, believe that prolapse of the cord is part of the hazard inherent in breech delivery. It is evident that we cannot compare fetal mortality rates from different clinics unless the standards are the same.

In an effort to ascertain the fetal risk inherent in breech delivery, we have analyzed 708 cases of primary breech delivery occurring on the Obstetrical Service of Bellevue Hospital during the ten years from June, 1934, to June, 1944. Internal podalic versions followed by breech extractions are not included, and cesarean sections are considered separately. During this period there was a total of 15,398 deliveries, giving an incidence of breech presentation of 4.6 per cent. All cases were delivered by the resident staff, with the assistance of a member of the visiting staff, when special difficulties appeared probable.

Methods of breech delivery are classified on this service as follows: (a) *Spontaneous breech delivery*, a term used for the cases in which the breech is quickly and spontaneously delivered without any manipulation by the doctor. This usually occurs only with small babies. (b) *Assisted breech delivery*, in which the birth is allowed to proceed spontaneously up to the appearance of the umbilicus, after which assistance is given for the delivery of the shoulders and

External cephalic version should be attempted repeatedly, but no undue force and no anesthesia are to be used.

A systematic outline for the management of breech delivery is given, but each case must be evaluated individually.

The important steps in breech delivery are: (1) prompt recognition of abnormal labor, (2) delivery if no descent for one hour and cervix is completely dilatable; (3) deep surgical anesthesia, (4) deliberation in delivery, (5) deep episiotomy, (6) Potter technique for delivery of shoulders, (7) the Celsus-Wiegand-Martin maneuver for delivery of the head or combined with forceps.

Cesarean section should be used more frequently in primiparas at term with large babies presenting by the breech.

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TABLE II. CALCULATION OF CORRECTED FETAL MORTALITY RATE

	CORRECTIONS	NO. OF CASES	STILLBIRTHS AND NEONATAL DEATHS	TOTAL NO. OF CASES	TOTAL STILLBIRTHS AND NEONATAL DEATHS	FETAL MORTALITY RATE, PERCENTAGE
Totals				708	220	31.0
	Nonviable infants	110	110			
Remainder				598	110	18.4
	Premature infants	174	68			
Remainder				424	42	10.0
	Twins	36	9			
Remainder				388	33	8.5
	Prolapse of cord	13	1			
Remainder				375	32	8.5
	Maceration of fetus	6	6			
Remainder				369	26	7.3
	Congenital defects	5	5			
Remainder				364	21	5.8
	Pre-eclampsia and eclampsia	5	0			
Remainder				359	21	5.8
	Premature separation of placenta	2	1			
Remainder				357	20	5.6
	Placenta previa	1	0			
Remainder				356	20	5.6
	Hemorrhagic disease of newborn	1	1			
Remainder				355	19	5.4
	Icterus gravis	1	1			
Remainder				354	18	5.1
	Miscellaneous	2	2			
Final remainder				352	16	4.5

Table II. In calculating the risk of breech delivery per se, we have excluded cases with the following complicating factors which affect fetal mortality.

*Nonviability.*—Nonviable infants are defined on this service as infants born before the twenty-eighth week of gestation and weighing less than 3 pounds. There were 110 such births with 110 deaths—a mortality rate of 100 per cent. The fetal mortality rate after correction for these cases was 18.4 per cent.

*Prematurity.*—A premature birth is defined on this service as occurring between the twenty-eighth and thirty-eighth week of pregnancy, the infant weighing between 3 and 5 pounds. There were 174 premature infants delivered of which 68 died, giving a premature fetal mortality rate of 39 per cent. The fetal mortality rate after this additional correction was 10.0 per cent.

*Presence of Twins.*—Breech presentations in twins often present additional complications such as maternal toxemia, premature separation of the placenta, uterine atony, and domination of the common circulation by one twin. As suggested by Tompkins,<sup>10</sup> the first twin eliminates much of the danger of delivery for the second twin by stretching the birth canal. There were 36 breech deliveries occurring in twins with nine fetal deaths, giving a gross fetal mortality rate of 25 per cent. The fetal mortality rate after this further subtraction was 8.5 per cent.

TABLE I. CORRECTED FETAL MORTALITY RATES OF VARIOUS AUTHORS

AUTHOR	YEAR OF PUBLICATION	FETAL MORTALITY RATE, PERCENTAGE
Caldwell and Studdiford	1929	11.11
Cannell and Dodek	1934	6.75
Macafee and McClure	1937	6.10
Mohler	1938	5.50
Siegel and McNally	1939	12.10
Patton and Mussey	1940	3.77
Hawker and Soule	1940	4.81
Goethals	1940	7.40
Hansen	1941	0.80
Waters	1942	11.20
Tompkins	1943	2.70
Moore and Steptoe	1943	12.80

head. This is the usual procedure for breech delivery on the service unless definite indications exist for breech extraction. Both shoulders are delivered anteriorly if possible, but, if difficulty is encountered, the posterior shoulder is delivered as such. The aftercoming head is delivered by either the Mauriceau-Smellie-Veit or Wigand-Martin maneuver. If these fail, Piper forceps are used. (e) *Breech extraction*, in which the operative interference is commenced before the passage of the breech over the perineum. The procedure is carried out on this service only for specific indications, the chief one being prolongation of the second stage.

Analgesia in the first stage of labor consisted, during these years, in the more or less routine use of nembutal and scopolamine. Demerol was utilized in certain cases in the last year covered by the study. Nitrous oxide and oxygen were used in the second stage up to the birth of the umbilicus, following which the patient was anesthetized with ether on an open cone. Breech extractions were performed throughout with this form of ether anesthesia.

Most of these cases were patients of the prenatal clinic, but a fairly large proportion were seen only after the onset of labor. Stereoscopic x-ray plates, in accordance with the Caldwell-Moloy technique, were employed to aid in the diagnosis of the pelvis whenever there appeared the slightest indication. In recent years all primiparas with breech presentations have been x-rayed.

It has been a policy of the Bellevue Service to perform prophylactic external cephalic versions after the thirty-sixth week of gestation. The patient is placed in Trendelenburg position, and the version is attempted without anesthesia. If the breech cannot be turned easily, further manipulations are deferred. During the period of this study there were 91 recorded attempts to perform external cephalic version, of which 56 cases, or 62 per cent, were successful. Others have reported success in over 90 per cent of the cases.<sup>7, 8</sup> In an analysis of 2,269 successful versions done by various authors, Siegel and McNally<sup>9</sup> have concluded that carefully done external versions result in few accidents and a good outcome for the fetus. Our experience has been the same.

### Complications in Breech Delivery

In this series of 708 breech deliveries there were 220 deaths, giving a gross fetal mortality rate of 31.0 per cent. Our analysis of these 220 deaths appears in



TABLE IV. ANALYSIS OF SIXTEEN UNCOMPLICATED BREECH FETAL DEATHS

PAR- ITY	BIRTH WEIGHT	X-RAY	PELVIS		MEASUREMENTS	TYPE OF DELIVERY	RESULT OF BABY	AUTOPSY	COMMENT
			TYPE						
P.	6 lb. 15 oz.	Yes	Anthropoid with <i>narrow inlet</i>	Not recorded	Breech ex- traction	Lived two hours	Bilateral tentorial lacerations with subdural hemorrhage	Slight disproportion	
P.	7 lb. 2 oz.	Yes	Gynecoid with <i>poor outlet</i>	A.P. = 10.8 cm. Trans = 11.6 cm. Spines = 9.0 cm.	Breech ex- traction	Died first day	Bilateral lacerations of tentor- ium with subdural hemor- rhage	Slight disproportion	
P.	6 lb. 9 oz.	Yes	Gynecoid	A.P. = 12 cm. Trans = 12 cm. Spines = 10.5 cm.	Breech ex- traction	Stillbirth	Bilateral tentorial lacerations with subdural hemorrhage		
P.	7 lb. 3 oz.	Yes	Gynecoid with <i>anthropoid fore- pelvis and only fair outlet</i>	A.P. = 12.5 cm. Trans = 11.8 cm. Spines = 9 cm.	Breech ex- traction	Stillbirth	Fracture dislocation of neck. Bi- lateral tentorial lacerations with subdural hemorrhage	Slight disproportion	
P.	10 lb.	Yes	Gynecoid	A.P. = 12.2 cm. Trans = 13 cm. Spines = 11 cm.	Breech ex- traction	Stillbirth	Laceration of right tentorium with subdural hemorrhage	Slight disproportion	
P.	8 lb. 3½ oz.	Yes	Gynecoid with <i>narrow outlet</i>	A.P. = 12 cm. Trans = 13.5 cm. Spines = 10.8 cm.	Breech ex- traction	Stillbirth	Bilateral tentorial lacerations with subdural hemorrhage	Slight disproportion	
P.	7 lb. 10 oz.	Yes	<i>Small</i> gynecoid	A.P. = 9.4 cm. Trans = 10.2 cm. Spines = 8.5 cm.	Breech ex- traction	Stillbirth	Bilateral tentorial lacerations with subdural hemorrhage	Slight to moderate disproportion	
P.	7 lb. 14½ oz.	Yes	Gynecoid	A.P. = 9.9 cm. Trans = 11.4 cm. Spines = 9.7 cm.	Breech ex- traction	Stillbirth	Aspiration of amniotic fluid		

*Prolapse of the Cord.*—There were 36 prolapsed cords in the total 708 cases—an incidence of 5.1 per cent. Among 388 cases of single mature breech births there were 13 prolapsed cords—an incidence of 3.4 per cent. Both of these figures contrast strongly with our vertex deliveries. During the years of this study, there were 14,255 vertex deliveries (excluding nonviable births) with 50 prolapsed cords—an incidence of only 0.35 per cent. Prolapse of the cord occurs, then, over ten times as often in breech as in vertex presentations.

Although it occurs less frequently, prolapse of the cord in a vertex presentation is much more serious than in a breech presentation. Thus, of the 50 prolapsed cords in vertex deliveries, 38 were in term cases. Of these 38, there were 20 fetal deaths, giving a fetal mortality rate of 53 per cent in term vertex deliveries with prolapsed cord. Among the term breech deliveries there were 13 prolapsed cords with one fetal death—a fetal mortality rate of 8 per cent. Therefore, fetal death will occur over six times as often with prolapsed cord in vertex deliveries as in breech deliveries. This difference is probably due to the fact that there is greater compression of the cord by the hard head than by the softer, smaller breech.

In spite of the great frequency of prolapsed cord in breech presentation and its relative safety, it cannot be discarded as a complication. We agree, therefore, with Macafee and McClure<sup>6</sup> and with Goethals,<sup>5</sup> who have also corrected for these cases. With the subtraction of cases with this complication, as well as those of the preceding groups, the fetal mortality rate remains 8.5 per cent.

*Other Complications.*—Six macerated term stillbirths were delivered in this series. In one case there were no fetal movements felt for two days before admission. Three of the six cases delivered with the cord around the neck, a possible cause of the intrauterine death.

Five cases of congenital fetal defects incompatible with life were eliminated from our figures. These anomalies included: exstrophy of the bladder with intestinal obstruction due to a large umbilical hernia, hydrocephalus necessitating a craniotomy on the aftercoming head, congenital cardiac anomalies, and two cases of spina bifida.

There were no fetal deaths attributable to maternal toxemia. Nevertheless, four cases of pre-eclampsia, and one of eclampsia were eliminated, since it was felt that these were complications which in general constitute an appreciable additional risk to the fetus.

Premature separation of the placenta was present in two cases and resulted in one fetal death. The fetal heart in this case was lost during labor, and examination of the placenta after delivery showed evidence of premature separation.

There was one case of placenta previa in the series, but this was followed by the birth of a living infant.

TABLE III. CORRECTED FETAL MORTALITY RATE IN PRIMIPARAS AND MULTIPARAS

	PRIMIPARAS		MULTIPARAS	
	NO. OF CASES	STILLBIRTHS AND NEONATAL DEATHS	NO. OF CASES	STILLBIRTHS AND NEONATAL DEATHS
Spontaneous breech delivery	5	0	3	0
Assisted breech delivery	131	2	174	4
Breech extraction	27	10	12	0
Totals	163	12	189	4
Corrected fetal mortality rate	7.4 per cent		2.1 per cent	

Severe hemorrhagic disease of the newborn and icterus gravis each resulted in one death during the neonatal period.

Two unusual complications were responsible for two fetal deaths. In the first case, although the fetal heart remained good throughout labor, an assisted breech delivery resulted in a stillbirth. At delivery, three tight loops of cord were found around the neck. Autopsy showed marked aspiration of amniotic fluid due to asphyxia. In the second case the patient was admitted with the cervix fully dilated and no fetal heart present. She was immediately delivered of a dead fetus. The cord was found to be unusually long, measuring thirty inches. It was felt that an occult prolapse of the cord had probably been present. Autopsy showed atelectasis and congestion of the lungs with moderate aspiration of amniotic fluid.

After excluding all the above complications, there is a remainder of 352 uncomplicated cases of breech delivery with 16 fetal deaths directly due to the breech presentation and delivery. This gives a corrected fetal mortality rate of 4.5 per cent. Since the corrected fetal mortality rate of all term deliveries on this service is 1 per cent, there is a four and a half times greater fetal risk inherent in breech delivery.

*Fetal Mortality Rate According to Parity.*—A comparison of the corrected fetal mortality rate in primiparas and in multiparas is shown in Table III. There were 12 fetal deaths in 163 uncomplicated primiparous breech deliveries—a corrected fetal mortality rate of 7.4 per cent. Of 189 uncomplicated multiparous breech deliveries, there were four fetal deaths—a corrected fetal mortality rate of 2.1 per cent. It is evident that the fetal risk in primiparas is over three times greater than in multiparas.

Ten of the deaths in the primiparous group occurred after breech extractions, and two deaths occurred after assisted breech deliveries. All the four deaths in the multiparous group occurred after assisted breech deliveries. This does not necessarily mean that the breech extractions as such were responsible for the fetal deaths. The essential cause is to be found in the reason for the extractions.

*Fetal Mortality Directly Due to Breech Delivery.*—An analysis of the 16 uncomplicated fetal deaths is given in Table IV.

In the primiparous group ten of the twelve fetal autopsies showed birth injuries—lacerations of the falx and tentorium cerebelli, intracranial hemorrhage, and fractures of the vertebrae. The other two autopsies showed marked aspiration of amniotic fluid, which in this clinic is considered anatomic evidence for the pre-existence of an asphyxial state.

Of the ten cases with birth injuries, eight were delivered by breech extraction, and of these eight, there was evidence of a slight to moderate disproportion between the fetus and the pelvis in seven cases.

There are two remaining cases of birth trauma in this group. They both followed assisted breech deliveries. In one of these cases the injury can be attributed to an incompletely dilated cervix which contracted about the head after the buttocks had passed through with ease. This is the only instance in which an incompletely dilated cervix played a major role in causing fetal death. The other case occurred in the delivery of a 7 pound, 12 ounce fetus through a pelvis which was considered clinically ample but was, unfortunately, not x-rayed.

In the multiparous group two of the four cases presented some degree of disproportion between fetus and pelvis. Autopsy on one of these cases showed evidence of birth trauma; the other showed aspiration of amniotic fluid. Of the remaining two cases, autopsy on one showed misuse of the Flagg laryngoscope as demonstrated by lung emphysema; autopsy on the other case was refused.

P.	7 lb. 14 oz.	Yes	Gynecoid	A.P. = 9.75 cm. Trans = 11.5 cm. Spines = 9.3 cm.	Breech ex- traction	Stillbirth	Aspiration of amniotic fluid
P.	8 lb. 3 oz.	Yes	Small gynecoid	A.P. = 9.0 cm. Trans = 11.0 cm. Spines = 10.5 cm.	Breech ex- traction	Stillbirth	Complete fracture T-4 vertebra. Moderate disproportion Laceration of falx with sub- arachnoid hem. Fracture of ribs
P.	7 lb. 3 oz.	Yes	Gynecoid	A.P. = 11.4 cm. Trans = 13.6 cm.	Assisted breech de- livery	Died first hour	Fractures of both parietal bones with subtentorial hem- orrhage
P.	7 lb. 12 oz.	No	Gynecoid	--	Assisted breech de- livery	Died first hour	Bilateral tentorial lacerations with subdural hemorrhage
M.	6 lb. 14 oz.	No	Gynecoid	--	Assisted breech de- livery	Died third day	Refused
M.	7 lb. 9 oz.	Yes	Gynecoid	A.P. = 10.5 cm. Trans = 11 cm. Spines = 9 cm.	Assisted breech de- livery	Died first day	Traumatic rupture of lung al- veoli. Emphysema of lung Flagg apparatus
M.	7 lb. 8 oz.	No	Ample with nar- row outlet	--	Assisted breech de- livery	Stillbirth	Tentorial laceration with sub- dural hemorrhage
M.	8 lb. 12 oz.	No	Ample	--	Assisted breech de- livery	Stillbirth	Aspiration of amniotic fluid Probable disproportion

*Cesarean Section.*—Cesarean section was performed in sixteen cases of breech presentation during the period of this study. The results are summarized in Table V. The indications were as follows: pelvic disproportion, 12 cases; cervical dystocia, one case; severe cardiac disease, one case; carcinoma of the rectum, one case; elderly multipara with no living offspring, one case.

All babies delivered by cesarean section were discharged well from the hospital. There was one maternal death occurring on the nineteenth postoperative day due to a retroperitoneal abscess with septicemia in a case of carcinoma of the rectum.

Twelve of the 16 cesarean sections were indicated because of pelvic disproportion. It is interesting to note that the disproportion in these cases was much more marked and easier to recognize than that found in our cases of delivery from below with fetal death. It seems, then, from the standpoint of the fetus at least, that it is an advantage to have definite rather than lesser degrees of disproportion.

### Discussion

Since eight out of 11 cases of birth injury show evidence of slight or moderate pelvic disproportion, it follows that any attempt to lower the fetal mortality rate must concern itself primarily with this group. Although other factors, such as uterine contractions, cervical dilatation, character of the soft parts, and the degree of extension of the fetus are important, the common denominator in these cases appears to be a minor degree of pelvic disproportion. Such a condition in vertex presentations would probably cause little effect, as the head would mold through the pelvis. Since the aftercoming head has no time to mold, there can be no trial of labor in breech delivery. The choice of procedure must be determined before the head reaches the pelvis.

The problem, then, is to determine the degree of pelvic disproportion beyond which cesarean section should be performed. Radiologic comparison of the size of the head and the pelvis is less satisfactory in breech than in vertex presentations.<sup>13</sup> The determination of pelvic disproportion in breech presentations still must remain an intelligent guess based on a clinical evaluation of the pelvis, the estimated size of the fetus, and careful x-ray studies of the pelvis as emphasized by Thoms and others.

In borderline cases, we must weigh the maternal risk in elective cesarean section against the fetal risk in delivery from below. In competent hands and with the advantages of penicillin, sulfonamides, and improved anesthesia, the maternal mortality rate in elective cesarean section can be kept to very low figures. In one recent report of 500 consecutive cesarean sections, the maternal mortality rate was 0.4 per cent.<sup>14</sup>

If a patient with slight to moderate degrees of pelvic disproportion is already in labor, slight additional information can be obtained by observing the ease with which the breech descends. If such a patient with good labor contractions has trouble pushing the breech forward into the pelvis, there will obviously be difficulty with the aftercoming head which has a larger circumference. But even if the breech descends rapidly, there is still no certainty that the head will do the same.

Combining the primiparas and multiparas, we find that of 16 fetal deaths in cases of uncomplicated breech delivery; 11, or 69 per cent, showed evidence of birth injury on autopsy. Of these 11 cases, eight, or 73 per cent, showed evidence of slight to moderate disproportion between fetus and pelvis.

Premature rupture of the membranes occurred in eight of these 16 cases. We feel that this did not contribute to our fetal mortality in any significant way, and only two instances of prolonged labor occurred with this complication. Both of these cases showed pelvic disproportion, and autopsy showed intracranial injury. In analyzing cases with premature rupture of the membranes Schulze<sup>11</sup> found that the fetal mortality rate in breech was only slightly higher than usual. Cannell and Dodek<sup>12</sup> stated that the duration of labor was not affected by early or late rupture of the membranes.

TABLE V. ANALYSIS OF SIXTEEN CESAREAN SECTIONS IN BREECH PRESENTATION

PAR-ITY	BIRTH WEIGHT	PELVIS			RESULT OF BABY	INDICATION
		X-RAY	TYPE	MEASUREMENTS		
P.	6 lb. 10 oz.	Yes	Android with poor midpelvis	A.P. = 10 cm. Trans = 12.5 cm. Spines = 9 cm.	Normal	Moderate disproportion. Poor configuration of pelvis
P.	8 lb. 11 oz.	Yes	Small anthropoid	Poor plates	Normal	Moderate to marked disproportion
P.	6 lb. 2 oz.	No	Clinically ample	--	Normal	Cervical dystocia
P.	6 lb.	Yes	Small gynecoid with android tendencies	A.P. = 9.5 cm. Trans = 9.5 cm. Spines = 8 cm.	Normal	Moderate disproportion
P.	8 lb. 11 oz.	Yes	Gynecoid with narrow forepelvis and outlet	A.P. = 10.3 cm. Trans = 11.4 cm. Spines = 8.3 cm.	Normal	Moderate disproportion
P.	9 lb. 6½ oz.	Yes	Android with flat tendency	A.P. = 8.5 cm. Trans = 11.5 cm. Spines = 8.5 cm.	Normal	Marked disproportion
P.	6 lb. 5 oz.	Yes	Platypelloid with fair midpelvis and outlet	A.P. = 8.5 cm. Trans = 12 cm. Spines --	Normal	Moderate disproportion
M.	6 lb. 13½ oz.	Yes	Gynecoid with marked android tendencies and poor outlet	A.P. = 9.9 cm. Trans = 10.2 cm. Spines = 9.2 cm.	Normal	Moderate disproportion, previous cesarean section
M.	10 lb. 1 oz.	Yes	Marked android with narrow forepelvis	A.P. = 9.5 cm. Trans = 10.8 cm. Spines = 8.5 cm.	Normal	Marked disproportion
M.	5 lb. 8 oz.	Yes	Gynecoid with good outlet	--	Normal	Cardiac
M.	8 lb. 9 oz.	No	Clinically ample	--	Normal	Carcinoma of rectum with obstruction of birth canal
M.	8 lb. 15 oz.	Yes	Platypelloid	A.P. = 9.4 cm. Trans = 12.3 cm. Spines = 10 cm.	Normal	Moderate disproportion
M.	9 lb. 7½ oz.	Yes	Android with platypelloid tendencies	A.P. = 8.3 cm. Trans = 12 cm. Spines = 9 cm.	Normal	Marked disproportion
M.	7 lb. 1 oz.	Yes	Small android	A.P. = 8 cm. Trans = 10.5 cm. Spines = 8.5 cm.	Normal	Marked disproportion
M.	6 lb. 4 oz.	Yes	Small gynecoid with platypelloid tendencies	A.P. = 9 cm. Trans = 12 cm. Spines = 9.5 cm.	Normal	Slight to moderate disproportion
M.	6 lb. 5 oz.	Yes	Gynecoid with good midpelvis and outlet	A.P. = 10.5 cm. Trans = 11.5 cm. Spines = 9.5 cm.	Normal	Elderly multipara; no living children

## MATERNAL OBSTETRIC PARALYSIS

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**M**ATERNAL obstetric paralysis, or traumatic puerperal neuritis, is a condition observed during the puerperium, and occasionally during labor. It is characterized by pain and paresthesias and a variable paralysis of one or both of the lower extremities. There have been several cases of obstetric paralysis recently at the Woman's Clinic of the New York Hospital and, because of a desire to direct attention to the importance of early diagnosis and treatment of this unfortunate complication of pregnancy, these cases will be recorded in some detail.

Nerve injury of the mother due to the trauma of labor has long been recognized, yet has received little attention in the textbooks of obstetrics, and the obstetric literature dealing with this disturbing injury is meager. This may be attributed to the fact that few, if any, cases are encountered in a lifetime of obstetric practice. Often these patients are under the care of a consulting physician, and their records may be lost to obstetric writings. Again, the injury may be of such a mild nature as to go unnoticed, or, as Barns observes, cases may be attributed to a functional cause when it is tempting to suggest that trauma has occurred to pelvic nerves.

### Symptoms

The objective and subjective findings in obstetric paralysis are not always constant. Pain during labor, referred along the course of the sciatic nerve, is the earliest sign. With the present-day widespread and liberal use of sedative drugs, and the introduction of caudal anesthesia, this symptom might easily be overlooked. As labor continues and uterine contractions become more intense, the pain increases in severity. Indeed, it may be associated only with the uterine contractions. Various paresthesias occur. The patient may complain of: "numbness," "dead feeling," "foot is asleep," "pins and needles," or of thermal changes. During this same period, spasmodic contractions of muscles and paralysis may be observed. In many cases the condition goes unrecognized until several days after delivery. The degree of nerve involvement also varies, but paralysis of the flexors of the foot, or "foot drop," is a rather constant finding. Careful examination, however, will show that other muscles of both the leg and thigh are paralyzed. The ankle and knee jerks may exhibit abnormalities, while sensory findings will range from almost normal to complete loss. In severe cases, atrophy and wasting of muscle groups will eventually follow.

### History and Etiology

In most of the literature, von Basedow (1838) is given credit for the first description of maternal paralysis. Churchill (1857) devoted an entire

There is only one way in which the fetal mortality rate from breech delivery can be appreciably lowered. Every primipara and any multipara with a history of difficult or premature deliveries, in which a breech is found that cannot be changed by external version, should be worked up clinically and radiologically. The size of the fetus should be estimated with care. On the basis of these studies, if slight to moderate disproportion is found to exist, an elective or early cesarean section is indicated.

### Summary and Conclusions

Seven hundred and eight cases of primary breech delivery occurring at Bellevue Hospital between 1934 and 1944 have been presented. In this series there were 220 stillbirths and neonatal deaths, or a gross fetal mortality rate of 31.0 per cent.

After deduction of the cases with various complications, there remained 352 normal breech deliveries with 16 fetal deaths, giving a corrected fetal mortality rate of 4.5 per cent.

Of these fetal deaths 11, or 69 per cent, showed evidence of birth injury on autopsy. Of these 11 cases eight, or 73 per cent, showed evidence of slight to moderate degrees of disproportion between fetus and pelvis.

The principal way by which the fetal mortality due to breech presentation may be lowered is the recognition of cases showing slight to moderate degrees of pelvic disproportion, and their treatment by elective or early cesarean section.

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and lie quite exposed, rendering them particularly liable to injury (Fig. 1). Hünemann felt that injury was due to pressure by the presenting part and not to the blade of the forceps. As cases were added to the literature, however, it became evident that the lesion was not so well localized as had first been supposed, and that other nerve fibers of the lumbosacral cord were also subjected to trauma. Thomas pointed out, in 1900, that the tibial nerve (formed from fibers of the anterior branches of the fourth and fifth lumbar, and the first, second, and third sacral nerves) also receives fibers by way of the lumbosacral cord. The tibial fibers lie anterior to the peroneal portion of the cord, the latter being dorsally placed against the bone along with nerve fibers supplying the gluteus medius and gluteus minimus muscles. As both Lindén and Tillman note, it is difficult to imagine pressure so balanced that it would injure the peroneal portion of the lumbosacral cord without affecting the tibial portion. Yet Kleinberg suggests that the sometimes peculiar distribution of motor and sensory symptoms may be due to pressure of varying intensity on the different involved nerve fibers. If individual anatomic variations are excluded, it seems reasonable to assume that all fibers of the lumbosacral cord are subjected to trauma, and that the peroneal fibers are chiefly affected because of their position, for the paralysis is constantly found in the distribution of this nerve.

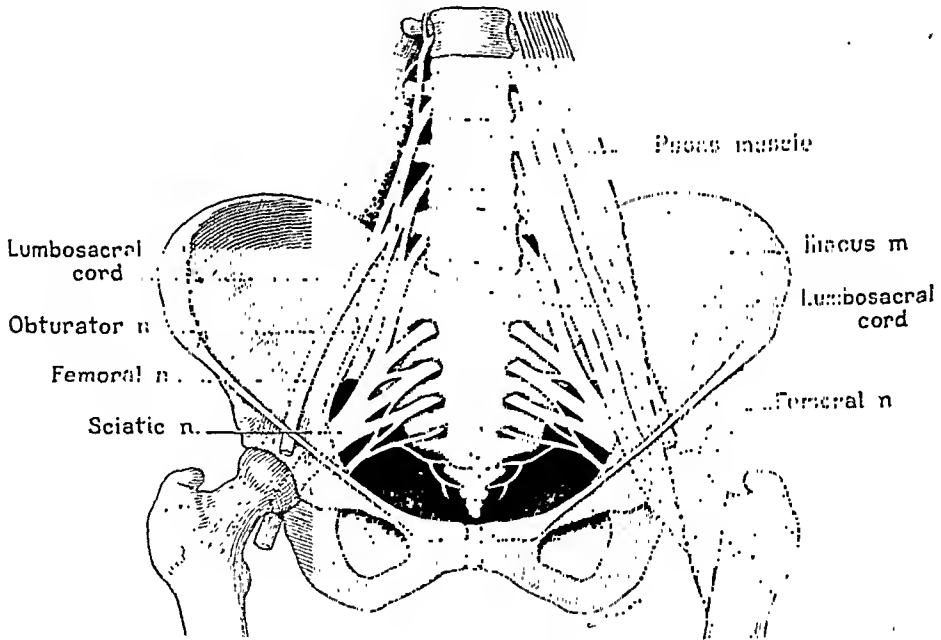


Fig. 1.—The relationship of the lumbosacral cord to the pelvis.

The pressure theory is not without critics. Lambrinudi feels that the true condition is one of traction on the lumbosacral cord. He quote Brooks, who concluded that during the first stage of labor there was a rotation backward of the sacrum, the axis being through the lower half of the articular facet, and that in some of these cases the excursion was as much as one-quarter inch. Since this is a measure designed to enlarge the anterior-posterior diameter of the pelvis at the inlet, it would not be unreasonable to assume that in a difficult labor the displacement would be even greater. On the other hand, the lumbosacral cord is known to be one of the tautest nerves in the body, and no explanation is offered for the rare occurrence of paralysis, especially the bilateral injury which would seem more likely were Lambrinudi's conclusions entirely correct.

O'Connell has recently (1944) offered another explanation. He believes that during pregnancy there occurs a relaxation of the lower intervertebral

chapter of his book to paralysis. He made a searching inquiry of the texts and periodicals, and communicated with many of the outstanding physicians of his time, only to report that his search for information concerning this condition had not been very fruitful. He refers to Smellie, Campbell, Ryan, Ramsbotham, Simpson, Romberg, Seanzoni, and others, and notes that the subject of paralysis is usually completely ignored, or, at best, brief mention is given. Although it is apparent that some difficulty was experienced at this time in dissociating nervous disorders accompanied by albuminuria, and conditions which today appear undoubtedly to have been traumatic paralysis, those writers who did express an opinion showed knowledge of the clinical picture and insight into the mechanisms involved in the production of the paralysis. Churchill quotes Ryan, who believed that some women, after the easiest as well as instrumental delivery, suffered paralysis of the lower extremity. Ramsbotham made the same observations, and added that it occurred sometimes when the labor had been of ordinary duration or even of unusual rapidity, but more frequently when the labor had been tedious and painful. Churchill records that both Ramsbotham and Campbell agreed that the palsy must be owing to the long duration of the head in the pelvis, from disproportion, and from the pressure which the muscles and nerves sustain during the passage of the head through the pelvis. Romberg suggested as a cause the direct pressure of the distended uterus or an ovary on the nervous plexes of the lower extremity. Doctor Simpson of Edinburgh, with whom Churchill was in communication, had observed states of local paralysis which were not associated with albuminuria. These writers were aware that they usually dealt with a partial paralysis of one extremity, and they had not seen a resultant permanent lameness.

In 1866 Beatty described a typical case of obstetric paralysis. His treatment consisted of "blisters along the course of the sciatic nerve." He felt that the paralysis may have been the result of "exposure to the noxious influence of puerperal fever," for that disease was rampant in the hospital at that time. Seanzoni (1867) recognized postpartum palsy and was careful to differentiate it from more serious conditions, such as meningitis. He admitted that some cases were probably due to pressure, but felt that since the paralysis did not appear until some time after labor, pressure was not the sole cause, and some more profound derangement was present. He further pointed out that collections of exudates about nerve trunks, or constriction of the superficial capillaries of the extremities with an overfilling of the pelvic blood vessels, might presumably produce pressure on nerve tissue and lead to the symptoms and signs observed.

Beginning in 1867, and for approximately a decade thereafter, articles appeared in the French literature on the subject of puerperal nerve injury. Of particular note is the work of Bianchi (1867). In 1902 Garrigues noted that, in some cases, intrapartum symptoms were so severe that the affected leg was thrown violently upward during a uterine contraction. Garrigues and Hirst felt that it was a generally contracted pelvis that especially predisposed to neuralgia, while in a flat pelvis the protruding promontory offered protection for the nerve trunks.

The present-day conception of maternal obstetric paralysis begins with Hünemann, who, in 1892, observed that the paralysis had a definite distribution; i.e., it affected exclusively or chiefly the muscles supplied by the external popliteal nerve. He explained this on anatomic grounds, noting that this nerve receives its fibers principally from the dorsal branches of the anterior primary divisions of the fifth lumbar roots; and that these fibers, after forming the lumbosacral cord, pass over the brim of the pelvis. At this point the fibers are in relation to the sacral ala, have emerged from under cover of the psoas muscle,

If the hypothesis is correct, the reports of a few cases of bilateral nerve involvement must be interpreted by other means. The majority of cases of nerve injury is seen in prolonged labors, usually ending with difficult forceps deliveries. It is possible that during attempts at delivery one oblique of the pelvis is substituted for the other and nerve injury occurs on both sides, or that the injury may be attributed to the forceps themselves, since they are often reapplied many times. Again, when the head is in one oblique and an ideal forceps application has been achieved, the fetal head is in apposition to one nerve trunk, while the posterior blade of the forceps is necessarily in apposition to the opposite nerve trunk. If, as Lambrinudi believes, the lesion is due to sacral rotation, bilateral injury is easy to visualize. It would follow, however, that bilateral injury should be of common occurrence, which it is not. Furthermore, Barns cites a case of puerperal neuritis in which the patient had an obliterated sacroiliac joint. The theory of sacral rotation is also offered as an explanation for the sciatic pain not infrequently observed in the latter months of pregnancy. One must continue the theory by claiming that this group of patients would be "potential palsy victims;" but this is not the case, for many who complain of antenatal sciatic pain experience an uneventful labor and puerperium. On the other hand, it cannot be denied that injury might presumably occur as a result of both pressure and traction due to sacral rotation.

### Occurrence

It is impossible to make a definite statement concerning the frequency of maternal obstetric paralysis other than to say it is of rare occurrence. Tillman's rather recent report (1935) of nine cases was based on 18,900 deliveries, while the seven cases here reported occurred in a series of approximately 45,000 deliveries.

### X-ray Studies

X-ray pelvimetry is not employed as a routine procedure at the Woman's Clinic of the New York Hospital, but in these seven cases we were fortunate in that x-ray pelvimetry had been performed for various indications. In addition, an x-ray review was performed post partum, after obstetric paralysis had been diagnosed.

### Report of Cases

CASE 1.—Mrs. M., a para 0, was delivered by midforceps of a 3,190-gram infant, in right occipitoanterior position, after a desultory labor of one hundred and twenty-one hours. X-ray pelvimetry showed: 11 cm., obstetric conjugate diameter; 11.5 cm., transverse diameter; 9.75 cm., interspinous diameter; and 11.25 cm., ischial tuberosities.

Impression: "Except for slight midpelvic contraction, this is a good pelvis. A large baby might well arrest in the midpelvis."

X-ray review: "This is a gynecoid pelvis with slight midpelvic contraction. The notch is narrowed, and the posterior ileum average. The promontory does not encroach on the posterior pelvic capacity. Because of the mid-pelvic contraction, the head would seek the posterior segment as it descended." During the latter part of labor the patient complained bitterly of pain in the thighs referred along the course of the sciatic nerves. The pain was accentuated

joints similar to those occurring at the pubic and sacroiliac articulations. Cases are cited where the diagnosis of a protruding intervertebral disc was eventually supported at operation. Some of these women were known to have had the lesion prior to pregnancy, while in others the initial symptoms occurred during pregnancy. O'Connell feels that the alteration in the lumbar joint structure, the postural changes incident to pregnancy, and the muscle straining of labor render a woman more prone to the development of an intervertebral disc lesion, and that this lesion is the cause of a certain proportion of cases of maternal obstetric paralysis.

The possibility of neuritis following localized abscesses and puerperal infection has been mentioned by Seanzoni, Winscheid, and others. Thomas quotes Lloyd, who considered the question in 1892 and concluded: "The tendency of more modern writers is to dissent from this view (the pressure theory), and to ascribe lesions of the sacral plexus and its branches to a septic inflammation, propagated directly to the nerve trunks from a metritis or a periuterine cellulitis." There are reported cases of infected abortion with subsequent pelvic abscess and paralysis of the leg localized to the common peroneal nerve. Rarer conditions, such as: localized bone or muscle changes, stirrup injuries, embolism, tumors, avitaminosis, poisoning, and hysteria are to be differentiated from true nerve injury and are outside the scope of this paper.

We conclude, as does Barns, that maternal obstetric paralysis is chiefly due to trauma of the lumbosacral cord by the fetal head, or by instruments. In many cases cephalopelvic disproportion exists. If, in addition, a pelvis is present in which the posterior ileum is short, the ala of the sacrum has only a shallow anterior concavity, and the promontory does not encroach on the capacity of the posterior segment, it seems reasonable that that portion of the vertex in relation to the ala can exert real pressure on the lumbosacral cord when the fetal head seeks an obliquity. The head, when it has assumed an oblique position, is in relation to only one sacral ala, and therefore to only one lumbosacral trunk. This would explain why the lesion is almost exclusively unilateral, and why, barring instrumental injury, it affects the lower extremity of the right side when the head seeks the right oblique of the pelvis. Conversely, the left lower extremity is affected when the head seeks the left oblique of the pelvis. As Barns explains, the head would exert its greatest pressure on the nerve cord at the time of engagement and at the height of a uterine contraction. Prior to this time there is no direct relationship between nerve and vertex. This would place the time for the appearance of pain and other subjective symptoms rather late in labor.

The possibility of forceps or other manipulations causing nerve injury has been indicated. Where this is the sole factor the compression would be of short duration, but the degree of damage would depend on the amount and the force of traction used. E. Mills has recently (1945) reported seven cases of nerve injury, and it is her opinion that in the majority of cases the use of instruments is the cause, while the minority is due to direct pressure of the fetal head. It is also possible that instrumentation only adds to pre-existing injury. Mere compression without severance of fibers interrupts the conductivity of nerve tissue, and the severity of damage is directly dependent upon the duration and the amount of force employed.

Impression: "The cephalopelvic relationship is fair to good at the brim, but poorer in midpelvis. The head will engage with good labor, but may well arrest as descent takes place, for the midpelvis is poor. Forceps will probably be necessary and difficult. If the head does not engage after a reasonable amount of labor, a section might be a wise choice."

X-ray review: "This is a very small gynecoid pelvis with a straight sacrum and average to narrow notch. The posterior ileum is short and the promontory does not encroach on the posterior pelvic capacity. In this pelvis the head must seek the posterior segment." The patient's labor was described as "hard," but no sciatic pain or paresthesias were experienced. Her course was without incident until the second postpartum day, when she first noticed numbness and tingling of the right foot which became increasingly severe, until, by the fifth day, she complained that her foot felt heavy. A neurological examination at this time revealed the following loss of power on the right:

Hip	Ankle and Toes
adduction—moderate	plantar flexion—moderate
Knee	dorsiflexion—complete
flexion—moderate	inversion of foot—complete
Reflexes	eversion of foot—complete
ankle—slightly diminished	
plantar—diminished	
toe stretch—absent	



Fig. 3.—Right leg. Impaired sensation to light touch. Hypersensitive to pin-prick. (Case 2.)

The sensory impairment is illustrated in Fig. 3.

A diagnosis of obstetric paralysis was made and treatment instituted at once. After two weeks, the paresthesias had disappeared, dorsiflexion of the foot was weak, and dorsiflexion of the toes was still impossible. Three weeks after delivery the patient was able to walk with a leg brace, which she was able to discard after the twelfth week. When last observed, fourteen weeks post partum, she was able to walk without difficulty. She complained, however, that the right leg felt weaker and tired easier than the left leg.

during uterine contractions. Paresthesias and paralysis of the right leg were noted just prior to delivery. Loss of power was chiefly on dorsiflexion of the foot, and internal rotation and adduction of the thigh. In detail, loss of power occurred in the right extremity as follows:

**Hip**

flexion—slight  
abduction—slight  
adduction—complete  
external rotation—slight  
internal rotation—marked

**Knee**

flexion—slight  
extension—slight

**Ankle and Toes**

dorsiflexion—complete  
plantar flexion—slight

**Reflexes**

knee and ankle—present  
plantar—decreased  
toe stretch—absent



Fig. 2.—Right leg. Impaired sensation to light touch. Hypersensitive to pin-prick. (Case 1.)

The sensory impairment is illustrated in Fig. 2.

A diagnosis of obstetric paralysis was made, and the treatment which is described below was instituted. One month after delivery the patient was able to walk with the foot braeed. The area of sensory disturbance had greatly decreased. Although there was no evidence of dorsiflexion of the ankle, there was slight but definite power of dorsiflexion of the great toe. At the end of five months, the patient walked without a limp and the braee was no longer required. The extremity could be moved in all directions without limitation of motion. Her complaints were confined to numbness of the right great toe and the appearance of a limp in the evening following an especially active day. When last observed, thirteen months post partum, she was entirely asymptomatic.

**CASE 2.**—Mrs. N., a para 0, was delivered by midforceps of a 3,070-gram infant, in left occipitotransverse to left occipitoanterior position, after a labor of twenty-six hours. X-ray pelvimetry showed: 9.5 cm., obstetric conjugate diameter; 11.25 cm., transverse diameter; 9.25 cm., interspinous diameter; 10.5 cm., ischial tuberosities.

X-ray review: "This is an average gynecoid pelvis with average sacrum and average to narrow notch. The posterior ileum is short, and the promontory does not encroach on the posterior pelvic capacity." Five hours prior to delivery the patient noted numbness of the entire right lower extremity. Immediately following delivery the numbness ceased, except in the region of the right great toe and adjacent foot. Some weakness of the right foot was also noticed. The patient made no mention of these symptoms until the sixth postpartum day, when she complained of numbness of the part and inability to dorsiflex the foot. A neurological examination revealed the following loss of power on the right:

Ankle and Toes  
dorsiflexion—moderate  
inversion—moderate

Reflexes  
knee—present  
ankle—present  
plantar—decreased  
toe stretch—absent

The sensory impairment is illustrated in Fig. 4.

After ten days of treatment the patient was discharged in good condition. At six weeks post partum she was entirely asymptomatic.

CASE 5.—Mrs. R., a para 0, was delivered by midforceps of a 4,060-gram infant, in right occipitotransverse to right occipitoanterior position, after a labor of ten and one-half hours. X-ray pelvimetry showed (Fig. 7): 11.0 cm., obstetric conjugate diameter; 13.25 cm., transverse diameter; 10.75 cm., interspinous diameter; and 11.5 cm., ischial tuberosities.

Impression: "The sacrum is flattened. This type of pelvis allows little room for engagement of the vertex."

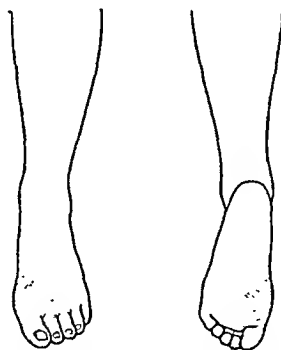


Fig. 5.—Left foot. Impaired sensation to light touch. Hypersensitive to pin-prick. (Case 5.)

X-ray review: "This is a platypelloid-android pelvis of average size. The sacrum is straight, the notch narrow, and the posterior ileum quite short. The promontory is flat and does not encroach on the posterior pelvic capacity." On the sixth postpartum day the patient complained that her left foot felt numb. She stated that immediately after regaining consciousness following delivery she noted numbness of the left leg distal to the knee. Since that time the numbness had decreased so that only toes one and two and the adjacent portion of the foot felt numb. A neurological examination revealed the following loss of power on the left:

Ankle  
reflex—decreased  
dorsiflexion—moderate  
plantar flexion—moderate  
inversion—moderate  
eversion—moderate

Great Toe  
extension—moderate  
flexion—moderate

CASE 3.—Mrs. T., a para 0, was delivered spontaneously of a 4,140-gram infant, in left occipitoanterior position, after a labor of seven and one-half hours. X-ray pelvimetry showed: 10.5 cm., obstetric conjugate diameter; 11.25 cm., transverse diameter; 10.75 cm., interspinous diameter; 12.0 cm., ischial tuberosities.

Impression: "This is a small anthropoid pelvis with a rather marked transverse contraction of the inlet. One would expect a persistent anterior or posterior delay in engagement, and a long labor. A large baby might offer great difficulty."

X-ray review: "This is a small anthropoid pelvis with a female notch and short posterior ileum. The promontory does not encroach on the posterior pelvic capacity. The presenting part must seek the posterior pelvis." The patient's labor was uncomplicated until two hours prior to delivery when, with each uterine contraction, she began to complain bitterly of low-back pain radiating down the posterior aspect of the right thigh. She felt tingling and complained of numbness in the right lower extremity. This was recognized as obstetric paralysis. While in the delivery room, the patient's legs were not allowed up in stirrups, but rather were supported by assistants. Treatment was begun immediately post partum. For the first three days there was tingling over the dorsal aspect of the right foot. Slight weakness was present on dorsiflexion of the foot and toes. By the fourth day recovery was complete. Nine months later the patient complained of occasional pain and tingling in the right leg. Eighteen months later the patient was delivered of a 4,300-gram infant by cesarean section. On questioning the patient during the last admission to the hospital, she found herself to be entirely well, but she had made the unusual observation that while in a shower bath "the drops of water feel different when they hit my right leg."



Fig. 4.—Right leg. Impaired sensation to light touch. Hypersensitive to pin-prick. (Case 4.)

CASE 4.—Mrs. D., a para iii, was delivered spontaneously of a 4,340-gram infant, in left occipitoanterior position, after a labor of eleven and one-half hours. X-ray pelvimetry showed: 11.25 cm., obstetric conjugate diameter; 13.0 cm., transverse diameter; 9.5 cm., interspinous diameter; and 12.25 cm., ischial tuberosities.

Impression: "Except for prominent spines this is a good pelvis."



The transverse of the inlet is narrow. Prognosis: vaginal delivery." X-ray review: "This is an average gynecoid pelvis with asymmetry on the left. The sacrum is average to straight, and the notch average. The posterior ileum is average, and the promontory does not encroach on the posterior pelvic capacity. The left sacral ala has a very shallow anterior concavity, while that of the right ala appears normal." (Fig. 6.) Three hours prior to delivery the patient began to complain of pain and numbness along the course of the left sciatic nerve. Slight loss of power on dorsiflexion of the left foot was demonstrable. Obstetric paralysis was recognized, and a careful midforceps delivery was carried out without incident. Treatment was instituted immediately post partum. A neurological examination revealed the following abnormalities on the left: weakness on dorsiflexion, inversion and eversion of the ankle, and definite weakness on dorsiflexion of the great toe. Sensory impairment was similar to that shown in Fig. 5. Improvement was rapid. The sensory disturbances were gone by the fourth postpartum day, and by the sixth postpartum day no motor weakness could be demonstrated. When last observed six weeks after delivery, the patient was entirely asymptomatic.

CASE 7.—Mrs. M., a para i, was delivered by low forceps of a 4,020 gram infant, in occipitotransverse to left occipitoanterior position after a labor of eleven and one-half hours. X-ray pelvimetry showed: 10.5 cm., obstetric conjugate diameter; 13.0 cm., transverse diameter; 10.5 cm., interspinous diameter; and 12.0 cm., ischial tuberosities.

Impression: "It is too early to give a prognosis concerning the cephalopelvic relationship. This is the sort of pelvis through which an average head will go with good labor. At present there is no disproportion, but patient has six weeks to go to term."

X-ray review: "A review of the x-ray reveals a straight sacrum, a promontory which does not encroach on the posterior pelvic capacity, and sacral alae with shallow anterior concavities." For a period of three hours prior to delivery the patient experienced great pain throughout the entire right leg. This pain was accentuated with each uterine contraction. One hour prior to delivery she was unable to move the leg. After an easy low forceps delivery, treatment was started. A neurological examination at this time revealed the following loss of power on the right:

Hip	Ankle
adduction—complete	dorsiflexion—complete
internal rotation—complete	inversion—complete
Toes	Reflexes
extension—complete	knee—slight increase
	plantar—decreased
	toe stretch—absent

The sensory impairment was similar to that illustrated in Fig. 5.

During the first five postpartum days there was definite improvement. Sensory disturbances were no longer present. However, after twenty-five days of hospitalization, she was discharged with a walking brace. Examination at the time of discharge showed that the patient was still unable to dorsiflex the foot. This has been our most recent case (discharged Jan. 26, 1946), and the prognosis must be guarded. It is our belief that the patient will probably show improvement during the next two years, but because she has apparently suffered rather marked damage to the lumbosacral cord, there will probably be some degree of permanent paralysis.

The sensory impairment is illustrated in Fig. 5.

The gait was only slightly affected by the injury. The patient was discharged on the eighth postpartum day with an elastic anklet for support. When observed six weeks after delivery, she complained of occasional pain in the left leg, as well as weakness of the part following a day of activity. After six months of observation the patient still notices weakness of the left great toe.



Fig. 6.—Pelvic x-ray of patient (Case 6) exhibiting the classical signs of maternal obstetric paralysis taken one-half hour prior to delivery. The asymmetrical sacrum is evident. The right sacral ala presents a deep anterior concavity; that of the left sacral ala is quite shallow. The fetal head is seen lying in right occipitoanterior presentation impinging on the left lumbosacral cord.

CASE 6.—Mrs. F., a para 0, was delivered by midforeeps of a 3,690-gram infant, in right occipitotransverse to right occipitoanterior position, after a labor of sixty hours. X-ray pelvimetry showed: 11.75 cm., obstetric conjugate diameter; 12.0 cm., transverse diameter; 9.5 cm., interspinous diameter; and 11.0 cm., ischial tuberosities.

Impression: "There is a flattening of the sacral ala on the left, and at the junction of the ileum and the sacrum there is a definite prominence of bone. The forehead of the fetus can be seen impinging on the area of bone discussed above.

jury. Barns points out that the early signs of lumbosacral cord compression should be watched for in trial labors. Should these signs appear, the dangers of instrumental delivery by the vaginal route should be kept in mind, and cesarean section might be considered the operation of choice. Unfortunately, as has been previously pointed out, these signs appear so late in labor that cesarean section does not seem wise. If forceps delivery is decided upon, the patient should be dealt with cautiously and delicately, using "art; not force." Tillman believes that "a multipara who presents herself with a previous history of difficult delivery, stillbirth, and recovery from nerve injury, should have a cesarean section." It would probably be more conservative to evaluate a subsequent pregnancy very carefully as regards to: pelvic mensuration, possible cephalopelvic disproportion, and the size and position of the fetus. Then, should it be evident that there was great likelihood of a repetition of nerve injury, cesarean section should be contemplated. This reasoning is borne out in Case 6, where an asymmetrical pelvis was discovered. The left sacral ala was found to have a shallow anterior concavity and the fetus in right occipitoanterior position. The right sacral ala was found to be quite normal with a rather pronounced anterior concavity. It is indeed tempting to suggest that this patient would suffer no injury during a subsequent pregnancy were the fetus in left occipitoanterior position.

Active treatment is designed to rest the extremity and support the foot in bed so as to prevent plantar flexion and over stretching of muscles. This may be done with pillows, sandbags, or padded footboards. In this respect, early recognition of the injury is of utmost importance. During this time gentle massage and passive motion are to be used so as to preserve muscle tone. Active movements may be encouraged, and the usual drugs are given for the relief of pain. When the patient is about one week post partum and has sufficiently regained her strength, galvanic stimulation of affected nerves may be instituted. Vitamin therapy is of doubtful value but, because of its claimed effect on nerve tissue, vitamin B may be used. Care must be exercised in guarding the patient against unnecessary falls when she again becomes ambulatory, and, should the injury prove of such severity that walking is extremely difficult, it will be necessary to resort to a walking brace.

### Prognosis

The prognosis is of necessity guarded, for it is difficult to estimate the degree of nerve damage until the patient has been under observation for a period of time. If, however, the condition is recognized early and appropriate treatment instituted without delay, a great deal of permanent deformity will be avoided. Recovery may be partial or complete, and may extend over a period of two or more years. It is true that the great majority of patients regain complete function, but it must be remembered that there is no measure of the "psychic trauma" that has occurred.

### Prevention and Treatment

The prevention of obstetric paralysis may not be easy. It is probably impossible to predict that a certain patient will suffer nerve injury during labor. X-ray pelvimetry reveals that the pelves of patients who have nerve



Fig. 7.—Pelvic x-ray of patient (Case 5) showing the usual findings in cases of maternal obstetric paralysis. The posterior ileum is short. The promontory is flat and does not encroach on the posterior pelvic capacity. The sacral alae present shallow anterior concavities.

injuries have a group of common characteristics (Fig. 7). But, in any series of x-ray pelvimetric studies, many pelves would be found which would exhibit these same characteristics, and yet the patients would not show any signs of nerve in-

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## Summary

1. Seven cases of maternal obstetric paralysis occurring in a series of approximately 45,000 deliveries at the Woman's Clinic of the New York Hospital are reported. All seven cases were personally observed by the author.

2. The majority of cases of obstetric paralysis will exhibit a combination of the following characteristics: primipara, prolonged labor, difficult forceps delivery, cephalopelvic disproportion. In addition, x-ray studies show that the pelvis will present certain characteristic features: a short posterior ileum, a sacral ala with shallow anterior concavity, and a promontory which does not encroach on the posterior pelvic capacity.

3. The patient who develops pain, paresthesias, and paralysis of either or both of the lower extremities during labor and/or the puerperium should have an immediate neurological examination.

4. A historical review of maternal obstetric paralysis is presented in an effort to demonstrate the development of the modern teaching.

5. The various theories as to etiology are discussed. The pressure theory, originally advanced by Hünemann, appears to be the most common cause of paralysis.

6. The prognosis as to degree and speed of recovery must be guarded.

7. The prevention of obstetric paralysis depends on recognition of the signs of lumbosacral cord compression, careful evaluation of the patient, and a correct decision as to the method of delivery.

8. Treatment consists of: support of the injured extremity, active and passive motion, galvanic stimulation, vitamin therapy, and the use of a walking brace.

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### Material and Technique

The material examined by the author consists of human umbilical cords at or close to term, all but one of the babies born alive. One cord was taken from a baby born alive at thirty-two weeks' gestation, but died sixteen hours after birth. Thirty cords were studied microscopically only—every constituent, such as Wharton's jelly, the blood vessels, their muscle, and elastic tissue being scrutinized. These cords were cut at various levels: near the navel, at the middle, and near the placenta. After formalin fixation, paraffin cross sections were made and stained with hematoxylin and eosin for routine observations, with van Gieson and Mallory stains to differentiate connective from muscle tissue, and with resorcin (Weigert) and orcein stains for detection of elastic tissue. The cords from the dead babies were utilized for the search of nerve tissue. The Schultze-Stöhr silver-stain technique on squeezed preparations was used for this purpose (Stöhr, 1921).

Twenty-five cords were studied grossly and examined for the presence of "valves," folds, or other peculiarities. Microscopic longitudinal sections were made of areas presenting special interest or questionable structures. For some of the deductions and new interpretations the author kept in mind the larger material which formed the basis for her previous publications (1936, 1943).

### Observations

*Macroscopic Study of the Vessels.*—The umbilical arteries differed grossly from other vessels of the body by their variable appearance throughout their course. On the outer surface of the artery which was studied in a fresh state after dissection from Wharton's jelly, there are grooves or furrows which occupy a part of the circumference of the vessel, and only occasionally the whole of it. These grooves or constrictions, partial or circular, demarcate the arteries into segments of various dimensions, and are a constant and striking feature of the vessel. They impart a peculiar and characteristic appearance to the artery which may resemble a string of pearls (Fig. 1). The lumina of the arteries differ widely in their dimensions at various levels. In some areas they are so narrow that only a small cannula can be inserted with difficulty. In other regions there are dilatations that may be as small as a millet seed, or as large as a pea or larger. Sometimes the dilated areas acquire a cylindrical shape, and then they may measure from  $1\frac{1}{2}$  to 2 cm. in length. These dilatations are known in the literature as noduli or gemmulae Hobokenii, deriving their name from the author who first described them (1669). Corresponding to the grooves on the outer surface, distinct prominences on the inner wall of the artery were seen when the vessel was studied either before or after fixation (Fig. 2). These protrusions were first described and demonstrated by the above-mentioned Hoboken (1669), who regarded them as true valves, a view much disputed by other investigators (M. Spivaek, 1936).

The dilatations, constrictions, and their corresponding internal folds were seen on blood vessels in their natural state of blood engorgement, but they could be made more distinct by injection of the vessel either with air or fluid. Frequently the furrows and dilatations were observed on cords not yet separated from the newborn and before dissection of the vessels from the Wharton's jelly; this is true especially for the umbilical vein. When a fixed artery was opened longitudinally there were, in addition to dilatations and folds, some areas which showed longitudinal stripes or corrugations, an anatomic peculiarity mentioned earlier by Stravinski (1876). The umbilical vein was studied by the author less extensively than the arteries. Here also partial or complete grooves were observed on the outer surface of the vessel. Often they were met at the point of

## THE ANATOMIC PECULIARITIES OF THE HUMAN UMBILICAL CORD AND THEIR CLINICAL SIGNIFICANCE

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**A**LTHOUGH the umbilical cord in man outlives its usefulness at birth it is, nevertheless, of paramount importance in intrauterine existence, serving as a vital link between fetus and mother. The fetus is virtually at the full mercy of this organ, the condition of which determines not only the welfare, but the very existence of its owner.

The lay mind somehow sensed the significance of this structure and surrounded it with an aura of magic and the supernatural in its folklore. By the appearance of the umbilical cord of the offspring attempts were made to foretell the fertility of its mother. The number of knots in the cord of the first-born served as an augury indicating the size of a family the mother is to have. The legitimacy of the child was determined by the specific gravity of the umbilical cord, its future virility by the size of its stump. Sterility or diminished fecundity were forestalled by tasting its blood or by eating its substance. The umbilical cord was worn as a talisman to protect its bearer from various sicknesses and misfortunes. The Japanese preserve the cord in a dry state and keep it in the family archive. It is given to the young bride to take it to her new home; it is placed in the coffin of a deceased son; it is buried instead of one who died on foreign land. The umbilical cord of the King of Uganda is so highly treasured that it is kept throughout his lifetime swathed in clothes, the number of which increases with the age of the king, so that eventually it acquires a human shape. Its eustodian ranks as an important Minister of State (Editorial in the *Brit. M. J.* 1912, and Busehan, 1934).

Leaving the supernatural to the superstitious, the scientists concerned themselves with the more tangible features of the cord and devoted much effort to its study. The umbilical cord of man was studied extensively, though not always accurately in the past. Its length, thickness, shape, tortuosity, the number of twists, their direction and mode of production, the blood vessels, their valves and innervation—all these were the object of study and dispute. A voluminous literature accumulated which almost escaped the English tongue. The present author feels that the discrepancies in the description of the anatomic elements of the umbilical cord and insufficient stress laid upon some important morphologic characteristics of its blood vessels furnish enough justification for further study. By offering a brief recapitulation of accepted observations and adding some of her own, she aims to clarify some obscure findings of her predecessors. She hopes that the presentation of this subject, much neglected in the English medical literature, is timely and, despite its modest practical application, will fill, perhaps, a didactic need.



*Microscopic Study of the Umbilical Cord.*—Histologically, the so-called “valves of Hoboken” present protrusions of the arterial wall in which all of its layers participate. They consist of longitudinal, oblique, and circular bundles of the media, both layers of which are appreciably thicker than in the adjacent portions of the vessel. On the innermost surface of these protrusions endothelial cells could be discerned. In some areas, marked on the outer surface of the artery by a deep constriction, a genuine doubling of the arterial wall with all its constituents could be observed (Fig. 3). In other areas one fold may consist merely of a convex thickening of the arterial wall, while the opposite one, whenever present, may represent an actual doubling of the vessel. In circular constrictions the protrusions of the arterial wall into the lumen, though identical in structure, varied in size as shown in longitudinal sections (Fig. 3).

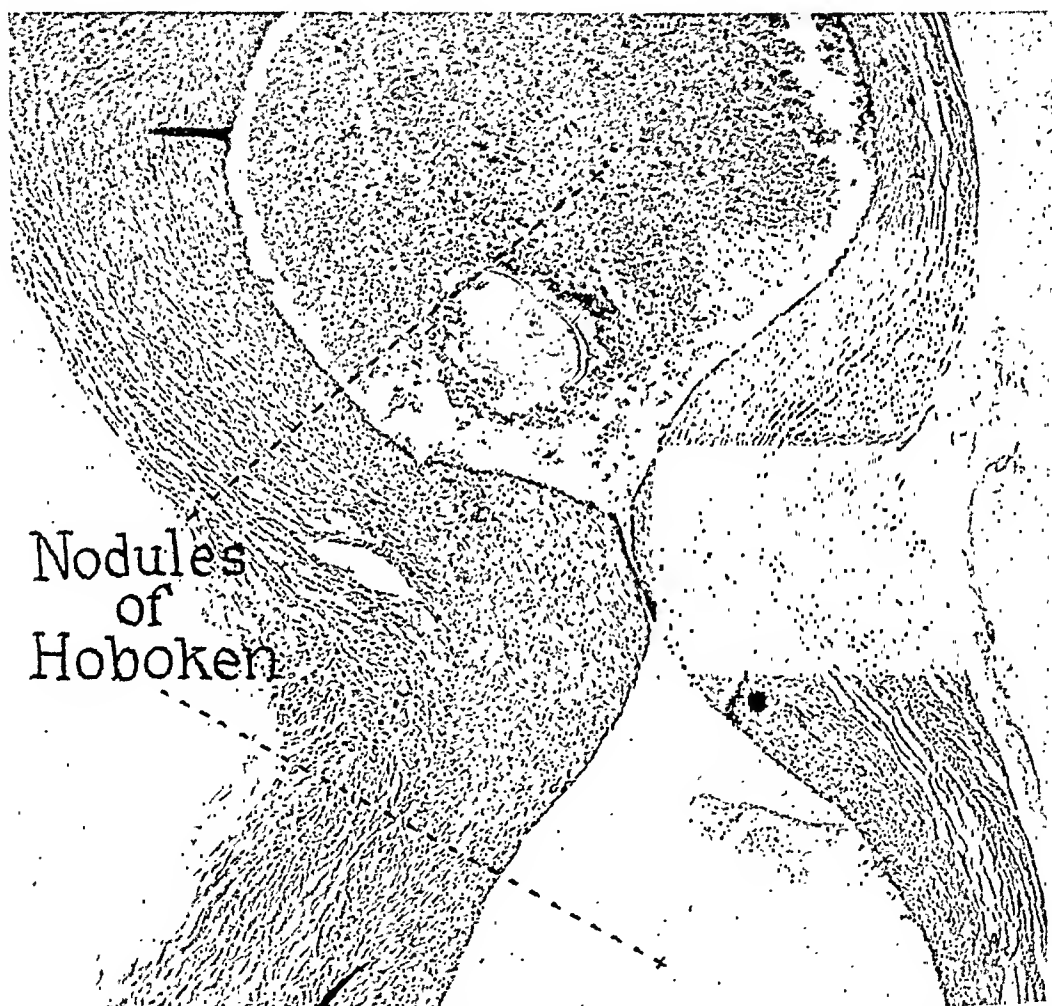


Fig. 3.—Microphotograph of an arterial segment in its natural state of blood engorgement, showing folds and nodules of Hoboken. Note the considerable thickening of both layers of the media in the folds and actual doubling of the arterial wall. The lumen of the vessel in this area is reduced to a slit. One of the nodules of Hoboken contains blood. (Longitudinal section, hematoxylin-eosin stain,  $\times 40$ .)

The nodules of Hoboken represent the stretches of artery in which the walls are thinned out (Fig. 3). The special stains for elastic tissue revealed a definite increase in the elastic components which attained their maximum at the thickest portion of the fold. The semilunar folds of the vein consist of one layer of musculature, the bundles of which assume various directions. In some instances actual doubling of the wall was observed.

sharp twisting of the vessel. The vein possesses a moderately thin wall which appears puckered after the emptying of its contents. When a vein showing invaginations was opened longitudinally, transverse or oblique semilunar folds were found which did not close its lumen, nor decrease it considerably. In many cases semilunar folds on the inner aspect of the vein were not marked on the outer surface by constrictions. In general the folds here were found with less frequency than in the arteries.



Fig. 1.—Roentgenogram of a segment of an umbilical artery, injected with an opaque substance. Note several constrictions, partial or circular, which impart to the vessel the appearance of a string of pearls.

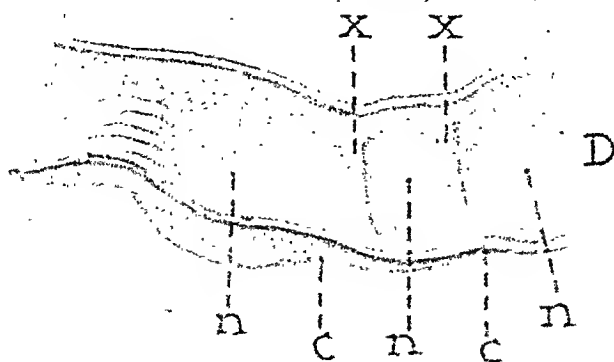


Fig. 2.—Drawing showing the folds of Heubach (x) in an arterial segment; corresponding constrictions on its outer surface; n, n, the dilations or partial Heubach (the dilations, constrictions and folds in this specimen were detected after the injection of the vessel with saline solution). (Reproduced from Fig. 1, M. Spivack) Anat. Rec. 66: No. 2, Sept. 1925, 1926.

"circular layer" used by many investigators, although with some qualification (Hennberg, 1902; Shordania, 1929; Popoff, 1938) etc., in reference to the outer portion of the media, is misleading. It is evident from the description given above that in the author's material no evidence could be found to corroborate the statement that the arteries possess three muscle layers, inner and outer longitudinal, and middle circular, as was believed by Eberth (1871) and others. Herzog's view (1892) that there is only a circular layer, the bundles of which are arranged spirally in a manner similar to that of the heart, is antedated by Tait's (1876), who observed the double spiral arrangement of the muscle

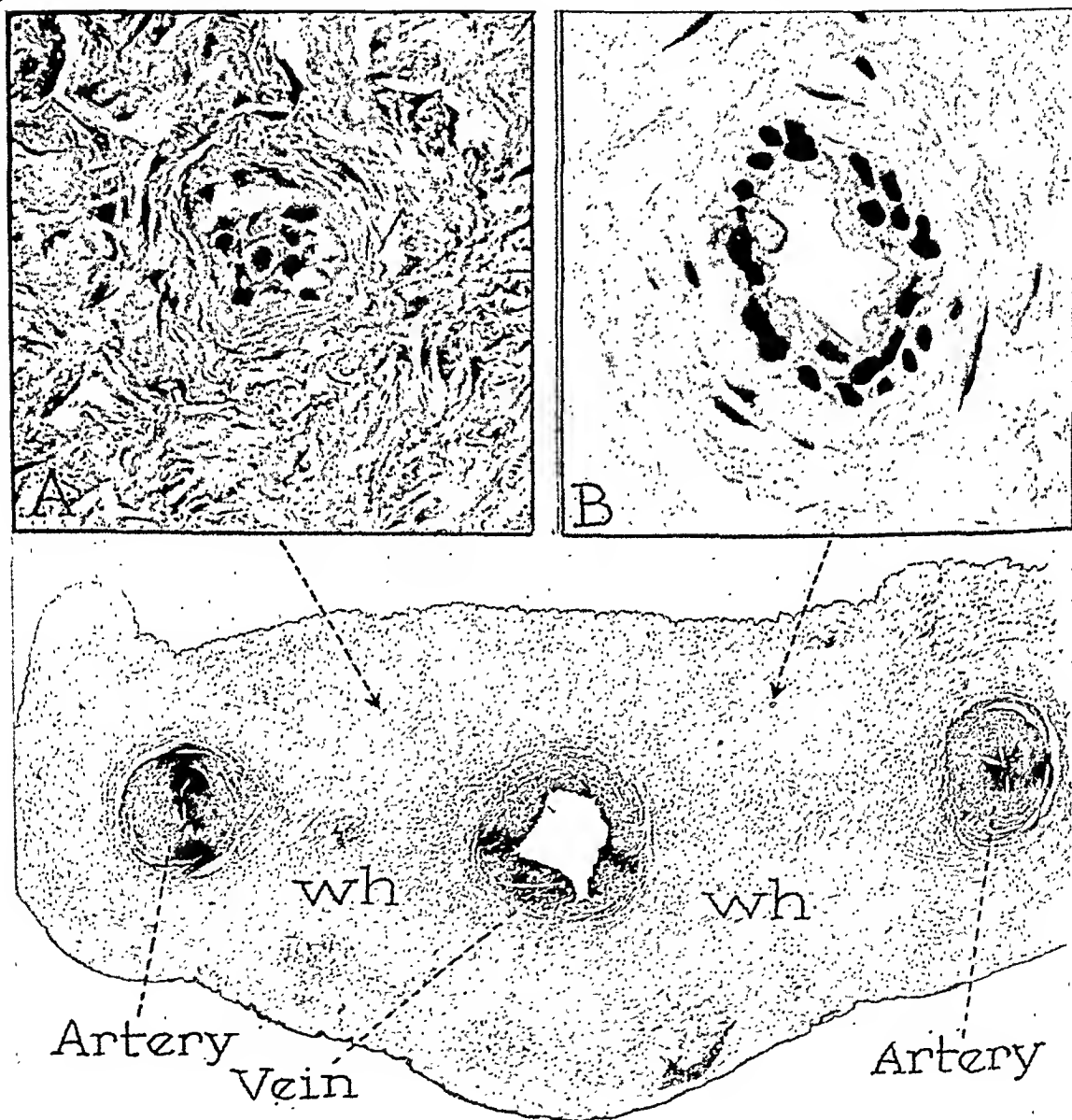


Fig. 4.—Microphotograph of a cross-section of a ripe cord, showing both umbilical arteries and the vein. Wh—Wharton's jelly; note the slit- and star-like lumina of the arteries (hematoxylin-eosin stain,  $\times 12$ ); Inserts A and B are vestiges of the allantois and the vitelline duct (the differential diagnosis between these structures is impossible in a single microscopic section). The cavity of one of the vestiges (insert A) is obliterated and lined with several layers of epithelial cells. The periphery consists of a concentrically arranged connective tissue layer. (Weigert stain,  $\times 480$ .) The Weigert stained microscopic section was selected for photography because it produced a better figure than a section stained with hematoxylin-eosin. The other vestige (insert B) presents a distinct cavity, lined with two layers of epithelial cells and surrounded by whorls of connective tissue. (Hematoxylin-eosin stain,  $\times 480$ .)

Unlike the "valves of Hoboken," the microscopic structure of the umbilical cord, as a whole, was studied extensively in the past, especial attention having been given to the fine architecture of its blood vessels; but even here a lack of uniformity in the description of their anatomic constituents prevails. The musculature of the umbilical blood vessels, the elastic tissue, the nerve tissue, all gave cause for disagreement. Every constituent of the cord, such as its sheath, Wharton's jelly, the blood vessels, their musculature, elastic tissue, was scrutinized by the present author, but especial emphasis was placed upon the architecture of the vessel's media. The blood vessels of the umbilical cord, which, as is well known, consist of two arteries and one vein, are embedded in a mucoid-like substance, known as Wharton's jelly. As is accepted universally, the sheath of the umbilical cord is derived from the amnion and resembles it morphologically. Wharton's jelly is composed of an irregular network of embryonic connective tissue in the meshes of which a varying amount of mucoid-like material is found. The cells are fusiform or stellate in shape, their nuclei are oval, but occasionally rod-like forms are seen. As a rule no nutrient vessels were present in the gelatin of Wharton, but three exceptions were noted. The nutrient vessels of the jelly were observed by other investigators, although at the region of the navel only (Minot, 1892). In the writer's material the umbilical end of the cords studied was never less than two inches from the navel, in accordance with the birth-room technique of their severance. Unlike other investigators, the present one never succeeded in detecting elastic tissue in Wharton's jelly, although modern methods of staining were used. In the cross sections of the umbilical cords the three vessels are often seen accompanied by another channel or strand which is considered by some authors as the relic of the vitelline duct and by others as that of the allantois. Among the latter, Küstner (1876) has traced this structure in a 6-month fetus to the urachus in an effort to prove its origin. The author has frequently seen a structure the center of which is made up of epithelial cells and its periphery of whorls of connective tissue, that because of their brighter staining reaction and coarser architecture contrast with the adjacent tissue. Sometimes the remnant retained its cavity which was lined with either flat or cuboidal epithelium. In the navel portions of 26 cords in which this structure was sought, it was found 16 times. Other investigators saw this remnant, which they considered as that of the allantois, either occasionally or almost regularly (Ahlfeld, 1876; Sabine, 1876; Minot, 1892; Runge, 1909; Wetzel, 1938). The present author possesses a specimen of the ripe cord in which both the vitelline and allantoic remnants can be seen (Fig. 4, inserts A and B). Morphologically, it is difficult to tell one from the other in a single microscopic section.

Turning next to the umbilical arteries, in the majority of cases these were found to be contracted in cross sections of the cord, their lumina having stellate, sickle-like, or triangular contours (Fig. 4). The inner surface of the arterial wall protrudes inward, forming elevations of various shapes and sizes. These elevations could be seen also with the naked eye on the slide or as the above-described longitudinal or oblique corrugations in the gross specimen. The arterial wall is composed of a one-layered intima and a thick muscular coat. The inner portion of the media consists of longitudinally arranged muscle bundles joined together by a dense fibrillar connective tissue stroma; circular bundles were discerned in this layer only occasionally. In the outer portion of the media there is a multiplicity of muscle bundles running in various directions and interwoven irregularly with each other to form a combination in which one or the other direction may predominate, more frequently that represented by the circular bundles. The connective tissue stroma of this layer is delicate and loose in texture, thereby differing considerably from that of the inner layer. The term

media and toward the periphery numerous circular bundles intertwine freely with the longitudinal ones. At no place in the media is a division into layers seen, contrary to the assertions made by other investigators (Shordania, 1929; Popoff, 1938; et.). A characteristic feature of the media is the loose consistency of its connective tissue stroma which is of such delicacy that the structure appears like a fine sieve or the film of a soap bubble on the verge of breaking. The character of this connective tissue, filling out the wide spaces between the muscle bundles, is responsible for the sponginess of the media. Like most observers the present writer did not see vasa vasorum in the umbilical vessels. The adventitia was found wanting by her and by several other students of the cord, although Virchow described an outer coat in the umbilical vessels as early as 1858, and Shordania used the term "adventitia" as late as 1929.

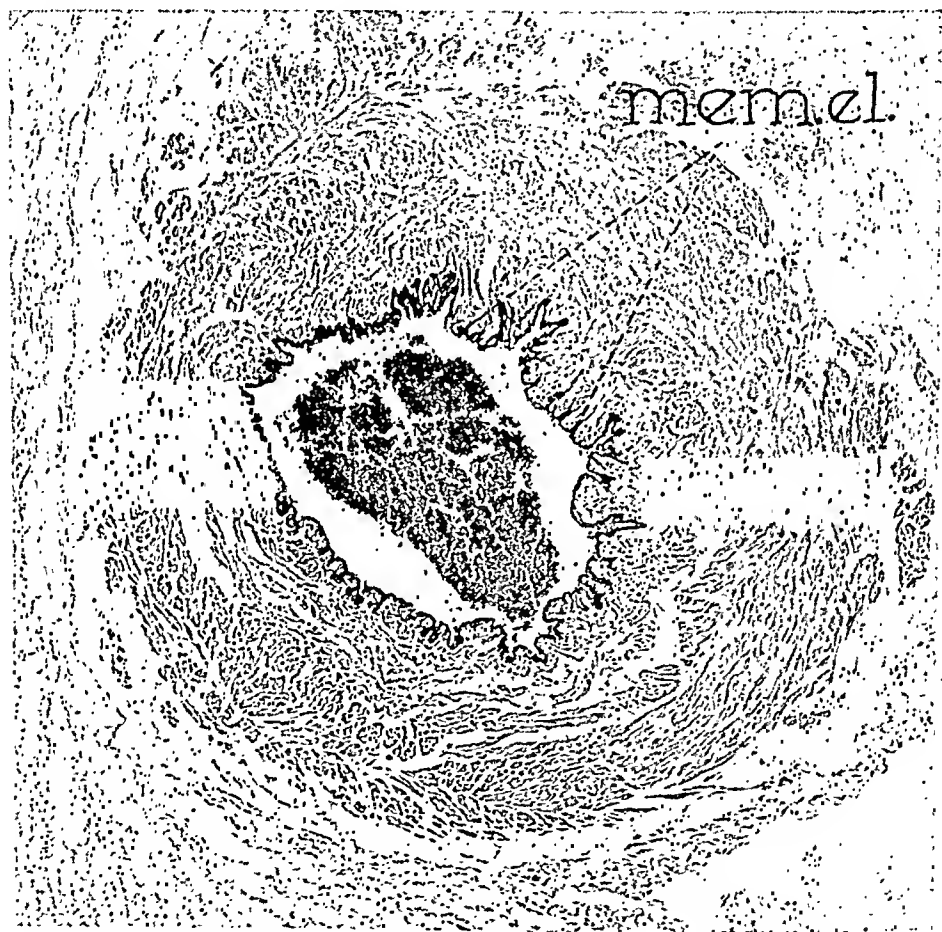


FIG. 6.—Microphotograph of an umbilical vein, illustrating the well-developed and sharply outlined membrane elastica interna (*mem. el.*) (cross-section, orcein stain,  $\times 47$ ).

It is interesting and puzzling that thus far no indisputable proof of the presence of innervation in the umbilical vessels has been found in the extensive literature. The discussion pertaining to this question began at the time of Galen and has occupied the minds of scientists during the past 300 years. A detailed review of the old literature was given by Schott over 100 years ago (1836); he was one of the early exponents of the view that nerves are present in the abdominal portions of the umbilical vessels and in the cord itself only near its attachment to the navel. He arrived at this conclusion by means of anatomic dissection, giving no microscopic evidence for his contention. Valentin

fibers, to which arrangement he ascribed considerable functional importance. Later (1935) von Hayek took up a detailed study of this question again, and he stresses the spiral and snail-like course of the muscle bundles in the media of the umbilical arteries.

The writer had no trouble finding elastic tissue in the umbilical arteries, the presence of which was denied in the past by some investigators. The umbilical arteries in contrast to other arteries of the same caliber do not possess a well-developed lamina elastica interna, claimed to be present in attenuated form by some authors (Shordania, 1929; Popoff, 1938) and others. But the arterial media contains a considerable amount of elastic tissue not as a continuous structure, but in the form of specks, clumps, or fine wavy fibrils (Fig. 5). On the other hand, in the vein the lamina elastica interna is well defined as a sharply

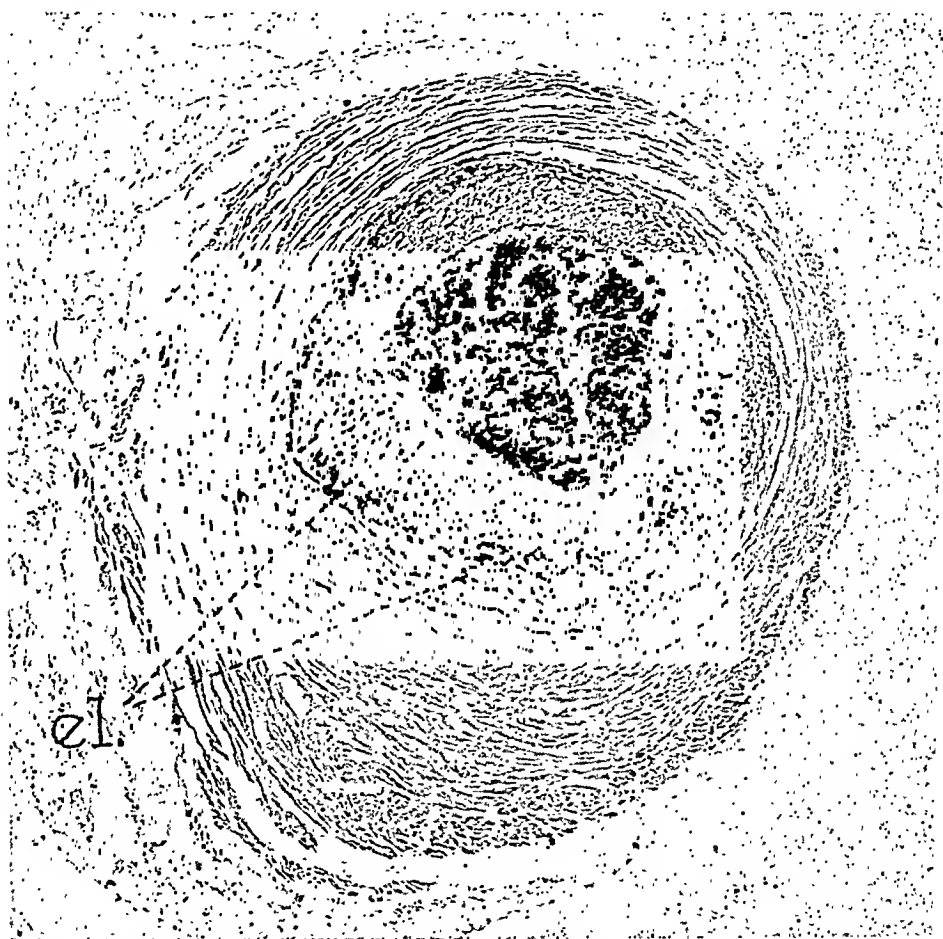


Fig. 5.—Microphotograph of an artery, showing the distribution of elastic tissue (*el*), as fine, wavy transverse fibrils within the inner portion of the media. Note the wide lumen of the vessel (cross-section, orcein stain,  $\times 47$ ).

outlined wavy structure underneath the intima (Fig. 6). Its presence here differentiates the vein from the artery. - Ordinarily the contracted artery with its slit-like lumen is differentiated easily from the wide vein by the naked eye or microscopically by the routine hematoxylin-eosin stain (Fig. 4). But in some specimens the differential diagnosis would have been difficult if not for the presence of the lamina elastica interna (Compare Figs. 5 and 6).

The distribution of muscle bundles in the vein differs from that of the artery. Although the muscle fibers immediately under the intima run principally in a longitudinal direction, quite often an addition of some circular bundles, which even predominate sometimes, could be detected. In the mid-portion of the

(1837) and Kölliker (1879) not only corroborated, but even extended the findings of Schott. These authors claimed that the proximal portions of the umbilical cord are supplied with a nervous apparatus, but like their predecessor they gave no illustrations to prove their assertions. In the present century a few investigators such as Mabuchi (1924), Dancz (1931), and others (complete literature, M. Spivaek, 1943), restudied the question. They claimed to have found nonmedullated nerves and nerve-endings within the arterial wall, a view which is strongly disputed by P. Stöhr, Jr. (1928, 1932, 1938). In a recent work (1943) the present author using the Schultze-Stöhr silver stain and the methylene blue supravital method was unable to find nerves in any portion of the umbilical cord proper. But availing herself of the same staining methods she has shown the presenee of nonmedullated nerves in the abdominal portions of the umbilical arteries, thus presenting for the first time the microscopic evidence

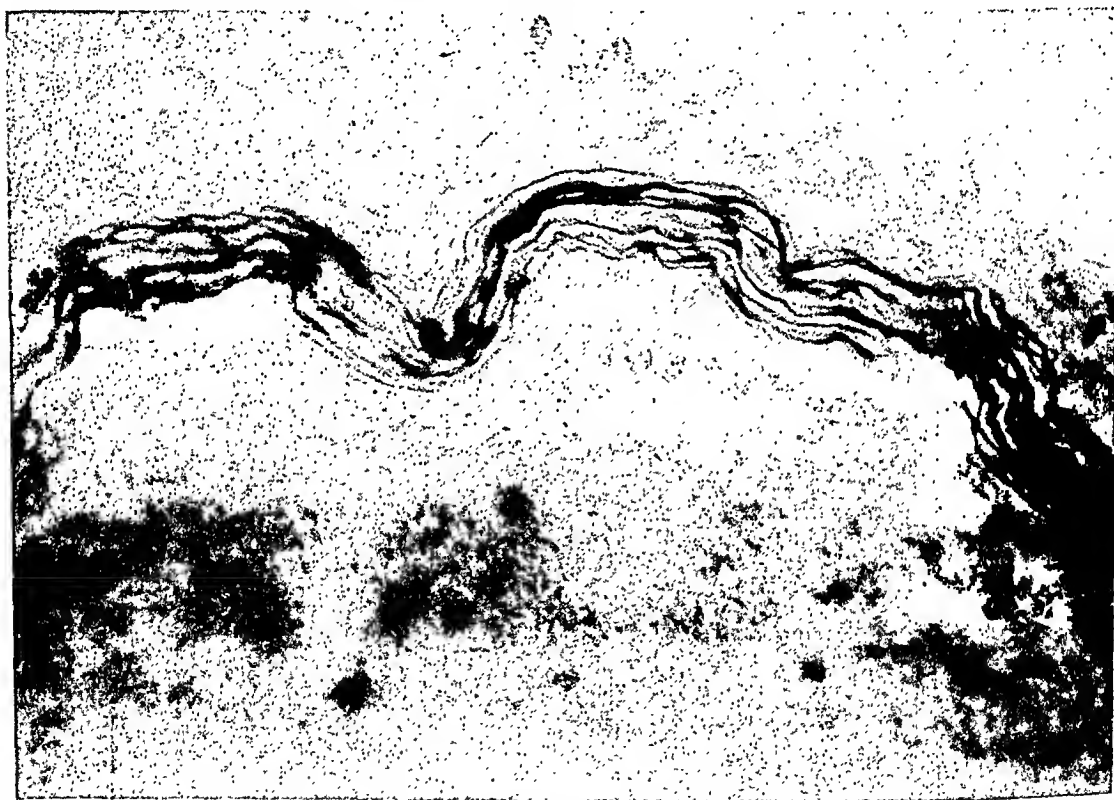


Fig. 8.—Microphotograph of the adventitia of the intra-abdominal portion of the vein; same fetus as above. The nerve bundle consists of several axons, some of them show clearly the varicosities. (Squeezed preparation, Schultze-Stöhr silver stain,  $\times 380$ .)

of the presenee of innervation in the vessels of this area. In the present communication, she is able to corroborate and amplify her previous positive findings by demonstrating again the presenee of nerves in the intra-abdominal stretches of the umbilical artery (Fig. 7). She can also show for the first time an illustration of nerve fibers in the adventitia of the intra-abdominal segment of the umbilical vein (Fig. 8). For clarity's sake the reader is reminded that the positive findings here concern only the abdominal portions of these vessels.

### Discussion

The author will not dwell at great length upon the theories concerning the function of the so-called "valvulae Hobokenii." Suffice it to say that she does not consider them to be true valves either from the anatomic or from the func-



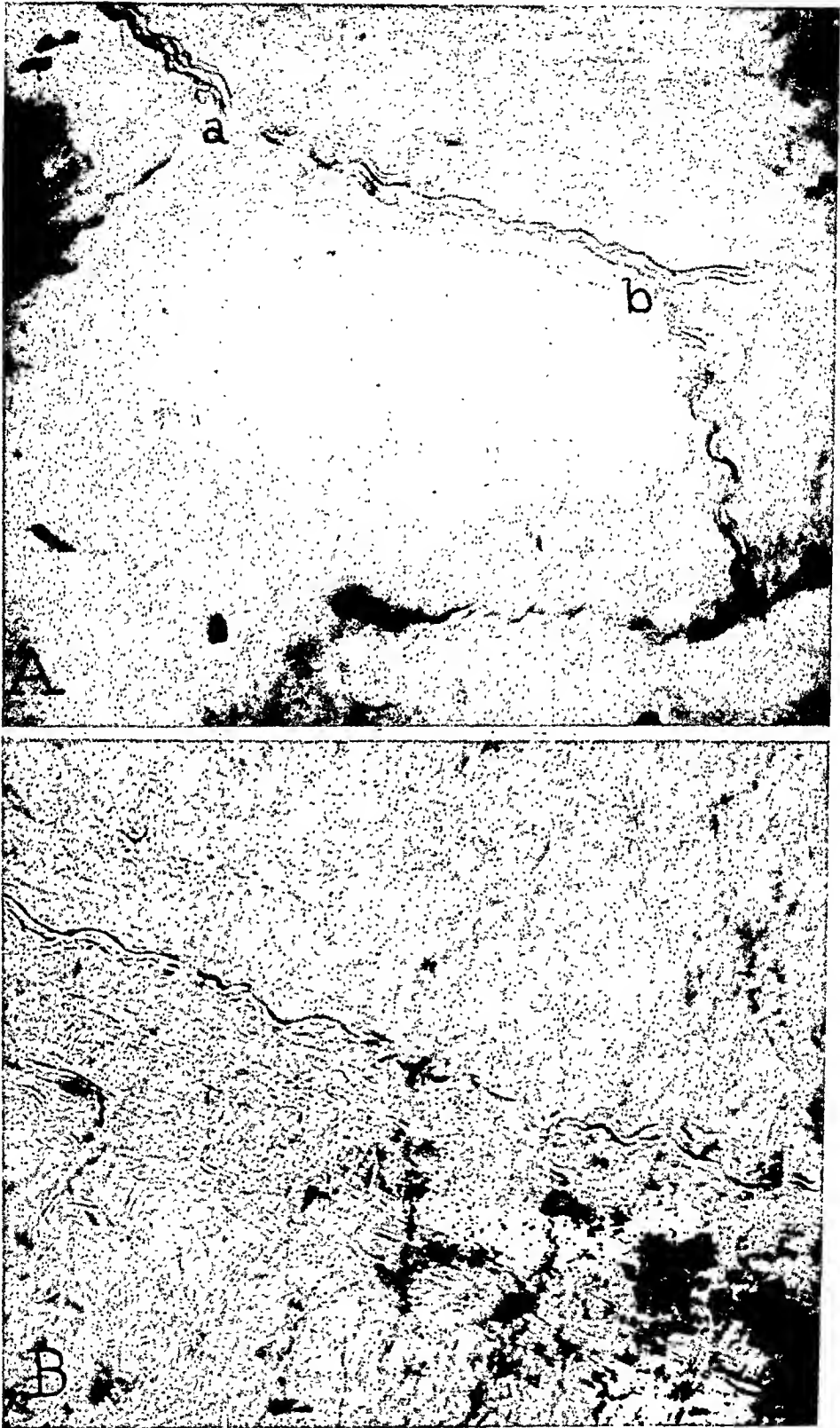


Fig. 7.—Microphotograph of the adventitia of the abdominal umbilical artery, obtained from a full-term stillborn. A. The main nerve trunk gives off branches at *a* and *b*. The axons are wavy and some of them exhibit varicosities. The paler appearing axons are out of focus; this thick, squeezed preparation was hard to photograph. (Schultze-Stöhr silver stain,  $\times 370$ .) B. Two fine nonmedulated nerve fibers alongside a nutrient vessel from the same section as A. Varicosities and beading well demonstrated. (Squeezed preparation, Schultze-Stöhr silver stain,  $\times 380$ .)



levels as well as the configuration of its wall. The essential prerequisite for this occurrence is the uneven build of the vessel's wall which thus responds to pressure from within.

It is an old and uniform observation that the umbilical arteries have a powerful media and a great capacity for contraction. Often their lumina are found to be slit-like and compressed almost to disappearance, especially in areas containing folds. According to Demelin (1897) the umbilical arteries after birth remained impervious under pressure up to 120 to 160, whereas the normal systolic blood pressure in the newborn fluctuates between 60 and 65 (quoted from Willson, 1922). A similar figure of 70 to 75 for the newborn's blood pressure was obtained by Haselhorst in 1929. He measured it in the umbilical arteries just after the birth of the child. The present author, as others, observed the difficulty of injecting the umbilical arteries soon after the delivery of the infant. As the literature reveals, the umbilical arteries possess great irritability and a tremendous capacity to contract powerfully in response to various stimulations. Mechanical, thermal, and electrical agents were used to evoke the contractility of the umbilical arteries. Here the author will touch merely upon this phase of the subject, not aiming at all to present the complete literature. Reeh (1925), by perfusing the umbilical arteries with gas containing fluids, proved their extraordinary contractility in response to stimulations with oxygen. He considers the oxygenation of the newborn's blood after establishment of its pulmonary respiration as the main factor in bringing about the closure of the umbilical arteries, thermal and mechanical influences playing only an assisting role in this process. von Hayek (1935), and others before him, also observed the characteristic ability of the umbilical arteries to narrow their lumina, almost to disappearance, but he ascribed this phenomenon to the snail-like course of the muscle fibers, an arrangement of the musculature which requires less contractile power for complete closure than a circular course of similar fibers. The custom of some primitive peoples for the mother to sever the umbilical cord with her own teeth (Engelmann, 1883) confirms the fact that the umbilical arteries have an intrinsic capacity to check their bleeding in unaided labor. Precipitated labors with complete rupture of the funis without hemorrhage from its stump is another clinical proof of this extraordinary feature. Experience since long ago has taught some clinicians that ligation of the cord is not paramount in the care of the stump. In Rachmanow's (1914) series of several thousand cases the cords were not tied and not a single newborn died from hemorrhage. He warns, however, that spontaneous cessation of pulsation of the cord and establishment of respiration are essential conditions before its severance. Many factors present during the delivery of the infant, such as the cooling of the cord after leaving the uterus, its handling by the attendant, its stimulation by the oxygenated blood of the breathing newborn, may bring about powerful contractions of the umbilical arteries. The folds of Hoboken, obstructing still further the lumina of the arteries, contribute to the perfection of the mechanism of their closure.

The well-known observation that the major portion of the placental blood can be drained back to the newborn in the first few minutes of its life has re-

tional point of view. Histologically, these structures are, as described above, protrusions of the arterial wall in which all of its layers participate. This description does not conform to the accepted conception of a genuine valve, which consists of an elastic-fibrous base covered with a layer of endothelium. Some of the older writers have pointed out correctly the inadequacy of these structures to obstruct the backflow of blood, as is supposed true valves would do. The author's experience with the injection method of the umbilical vessels is in complete accord with this view. At no time was a complete barrier to the flow of fluid obtained in only one direction. However, some hindrance to the stream was encountered when it met a constricted area. It is preferable, therefore, to refer to these questionable structures as folds, a term which does not carry the connotation of a specialized function. Mention may be made at this point that Spanner (1935) observed similar structures, which he designates "Polster," in the veins of the chorionic villi after injection with gelatine. He ascribes to them a sphincter-like function, aimed at slowing up the current of blood in the capillary network of the villi. This favors the heightening of the exchange of the metabolic products between the fetal and maternal blood streams. That a sphincter-like action might be exercised by a muscular structure is understandable from the morphologic point of view. Whether nature has intended them actually for the purpose postulated by Spanner is, of course, another matter.

When a constricted area of a fresh artery was subjected to procedures that destroyed, overstretched, or relaxed the circular bundles, obliteration of the constrictions and their corresponding folds resulted often. The integrity of the circular muscle fibers and their state of tonicity appeared to be essential in maintaining a given area in a state of constriction. The degree of the invagination on the outer surface of the vessel, in its turn, conditioned the depth of the fold on the inside. Whether the contractile muscular folds with their proved capacity for hindering a current of fluid in either direction possesses also a controlling influence upon the fetal stream through a sphincter-like action remains to be proved. It is conceivable that under physiologic conditions these muscular structures, alternately contracting and relaxing, may affect the caliber of the umbilical arteries in accordance with the circulatory needs of the fetus.

The question of the mode of production of these folds is intriguing and is subject to dispute. Several explanations were given by various investigators, but none was received universally. The torsion of the blood vessel in its course can be discarded justly as the cause of their production, since the constrictions and their corresponding folds are seldom seen at the point of its sharp turning. This is demonstrated particularly well by the x-ray photographs of the injected cords by which method they were detected in the initial stages of this study (Fig. 1).

The folds cannot be considered, as they were at one time, as artefacts in the sense that they might have been produced by the methods of the investigators. True enough the dilatations and constrictions were detected and best seen after the injection of the artery with either air or fluid, but they could be and were found also in the umbilical vessels in a state of natural blood engorgement. The blood that filled the vessel accentuated the difference in its caliber at various

The detailed study of the cord and its vessels, no matter how irrelevant to practical obstetrics at the time, was not altogether an idle pastime. At one or another phase in the history of the study of the umbilical cord, the data accumulated through centuries brought about a better understanding of the functions of this important fetal structure and placed some of the empirically acquired knowledge on a scientific basis.

### Summary

The umbilical vessels differ anatomically from other vessels of similar caliber in several essential ways: (1) in the presence of folds and nodules of Hoboken in the arteries and of semilunar folds in the vein; (2) in the absence of true valves; (3) in the peculiar distribution of elastic tissue; (4) in the strongly developed arterial media the powerful contractions of which are ascribed by some authors to the spiral or snail-like course of its muscle fibers; (5) in the absence of vasa vasorum and adventitia; (6) in a very delicate connective tissue stroma which contributes to the sponginess of the vein; (7) and lastly, in a nervous apparatus the existence of which thus far has eluded its positive demonstration.

It is a pleasure to acknowledge once more my gratitude and indebtedness to Dr. Otto F. Kampmeier, Head of the Department of Anatomy, for the invaluable help and generous counsel received from him throughout this study.

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ceived recognition in the recent literature (Windle, 1940). In 120 cases Haselhorst and Allmeling (1930) observed an average increase of 98 Gm. in the infant's weight by tying the umbilical cord after its cessation of pulsation. The first minute post partum furnished 51 per cent of the increase. Frisehkorn and Rueker (1939) approached the subject differently. They obtained a mean increase of 548.48 red cells per 1 c.c. mm. of blood in those infants whose tying of the cord was delayed until its pulsation had ceased. The material of 59 cases, thus treated, was compared with 333 others which served as controls. The fact that the newborn augments its blood volume soon after birth indicates that it receives more blood than it returns in a given period of time. It also means that a hindrance of circulation occurs which affects more the arterial than the venous path. The anatomic peculiarities of the arteries are sufficient in themselves to embarrass the blood stream flowing from the fetus; however, they are helped by other factors. During the first few minutes post partum the uterus contracts and compresses partly the placenta (Brandt, 1933). Obviously the blood vessels of the squeezed placenta, while furnishing resistance to the influx of blood, will not hinder the outflow. This furnishes an additional mechanism for obstructing the blood current returning *from* the fetus. On the other hand the umbilical vein has less contractile power than the umbilical arteries, and as a rule retains a fairly large lumen after its birth. Moreover, the compression of the placental vessels, while hindering the stream from the infant will not interfere—at least, in the first few moments post partum—with the current toward it. Then, too, the flow of blood to the baby is facilitated by the negative intrathoracic pressure, already established with the onset of respiration. It can readily be seen from the foregoing that nature has made generous provisions which render the umbilical arteries almost impervious to the blood stream soon after birth and thus forestalls its loss. Meanwhile it allows the venous path to function and thereby safeguards the circulatory interests of the child.

The author mentioned that in her previous work she had failed to find nerve tissue in the umbilical vessels of the cord proper. To her mind no conclusive evidence has been furnished by those who claimed positive findings. Although her criteria for diagnosing peripheral nerve fibers were rigid—not only varicosities but the presence of nuclei of Schwann's cells or a connection with a definite nerve bundle were the diagnostic requirements—they were not too rigid for detecting them in the abdominal portions of the same vessels. The author knows only too well from experience the difficulties in staining peripheral nerve fibers; she also appreciates the limitations of a negative findings. However, she feels that the existence of innervation in the umbilical cord proper must be considered not proved for the time being unless better evidence, based on stricter morphologic criteria, is adduced by the advocates of its presence. The great contractility of the umbilical arteries is hard to reconcile with the apparent lack of innervation in their major portion, even if the humoral theory of muscle stimulation and impulse conduction be evoked. In the face of the seeming absence of innervation, the *modus operandi* of stimulation, and contraction of the musculature of the umbilical blood vessels shall remain, for the present, a physiologic enigma.

## COMPOSITION OF THE HUMAN PLACENTA

### I. Proximate Composition

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THE complex mechanism for the nutrition of a human embryo, from the time that the fertilized ovum imbeds in the uterus to the time of birth when the fetus becomes an independent organism, must function through that highly specialized structure, the placenta. This organ, which has been likened to a "transitory liver,"<sup>1</sup> serves as a storehouse of building and maintenance materials from which the fetus, in a highly selective manner, draws its nutriment for growth and development. The placenta is indeed an intricate organ, varying so widely in different types of animals that its diverse forms seem only distantly related, yet its purpose is the same in all—to store and transport nourishment from mother to embryo and, in the mammalian type at least, to provide a mechanism for returning end products of fetal metabolism to the maternal blood.

Another means of protecting the embryo and, to a limited extent, for supplying nourishment and disposing of waste materials is provided by the amniotic fluid. Observations of Zangemeister and Meissl,<sup>2</sup> Makepeace, Fremont-Smith, Dailey, and Carroll,<sup>3</sup> and Cantarow, Stuekert, and Davis<sup>4</sup> on its physical properties and chemical composition have shown that, although the amniotic fluid may originate as a dialysate in equilibrium with the maternal and fetal body fluids, as pregnancy advances it becomes more diluted by fetal urine. It is noticeably high in uric acid, in which it exceeds the content of the maternal blood. The presence of meconium in the amniotic fluid and the phenomenon of fetal swallowing presupposes the contribution of some nutriment factors by this route. The presence of vitamin A in the amniotic fluid has been attributed to this meconium source, and small regularly occurring quantities of carotene have been assumed to come from the placenta.<sup>5</sup> Possibly owing to the alkalinity of amniotic fluid, vitamin C has not been found in it.<sup>5</sup>

During studies\* of the secretion and composition of milk by healthy mothers,<sup>6-14</sup> placentas were obtained from nine healthy multiparas, following normal deliveries at full term. The proximate composition of the placentas (wet and dry weights, protein, fat, ash, and energy) is presented in this paper. The lipid and vitamin distributions are given in following papers.<sup>15, 16</sup> The mineral analyses will be reported subsequently.

\*The investigation of the composition of the placenta was a part of studies of mothers during pregnancy and lactation, the composition of their milk, and the growth of their infants. Partial support for the investigation was given by the Nutrition Foundation, Inc.

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Boyd and Wilson<sup>29</sup> found that the placenta does not act solely as an organ of transmission, but absorbs lipoidal materials and then secretes them in suitable proportions. This regulatory role is substantiated by Neuweiler's studies<sup>30</sup> on thiamine storage and transmission, from which it is evident that the placenta controls the amount of thiamine so that the fetus receives a sufficiency and is protected from an excess.

According to Chang and Gaddum,<sup>31</sup> human placenta contains the richest supply of choline as acetylcholine in the body, with the exception of the spleen. This is derived wholly from the villous tissue of the fetal placenta, and the uterine muscle is very sensitive to it, the inference being that the acetylcholine of the placenta plays a part in the muscular contractions at birth. Needham<sup>32</sup> says: "It seems, on the whole, as if the embryo itself has little active part to play in mammals in the causation of birth . . . and that the arrangements have been relegated to the placenta and to an endocrine correlation in the maternal body."

Fetal nutrition depends to a large extent upon the efficiency of the transmission of material across the placental barrier. Only material which can be carried in solution by the blood and can pass through the semipermeable walls of the villi penetrates the placental barrier. Oxygen, carbon dioxide, and many chemical compounds of low molecular weight are transmitted through the membranes of all placentas. The red blood cells of the mother normally do not pass into the blood vessels of the fetus, nor those of the fetus into the mother's circulation. Proteins of large molecular structure are not transferred, but must be broken down into their component amino acids or proteoses. Fetal fat is synthesized from other lipid components passed from the mother's blood to that of the fetus and is quite different, chemically, from the body fat of the mother, being richer in palmitic and containing less oleic and stearic acids.<sup>33</sup> Antibodies do cross the placental membrane, hence the immunity of the infant. Certain virus diseases, too, are known to gain access. Vitamin D, ascorbic acid, thiamine, and riboflavin are known to be present in the human placenta and to be passed through it in regulated amounts, and vitamin A and carotene to a lesser extent.<sup>16</sup>

### Experimental

Each of the placentas analyzed was obtained in the hospital delivery room two to thirty-five minutes after the birth of a normal infant. After delivery, the placenta was placed in a 1,500 ml. specimen jar and transported to the laboratory. Five hundred milliliters of saline solution (0.9 per cent sodium chloride) was added and the excess blood and the umbilical cord were removed. Blood clots were removed by gentle squeezing with the hands, since the use of stirring rods or shaking was not successful or caused breaks in the placenta and consequent loss of internal tissue fluids. Two additional washings were made, using 250 ml. of saline solution for each. This procedure was sufficient to remove external blood.

After washing, the placenta was rinsed with double distilled water to remove the saline solution, and was allowed to drain for a few seconds but was not wiped. After weighing, it was put through a tin-plated grinder and the ground material collected in a two-liter evaporating dish. The grinder was washed with double distilled water, and the washings were mixed with the ground placenta to form a suspension. Aliquots of 80 to 90 Gm. of this suspension were placed in weighed 250 ml. centrifuge bottles, frozen at  $-50^{\circ}$  F. and dried to constant weight from the frozen state under high vacuum.<sup>34</sup> After the dry weight was recorded the samples were powdered, placed in amber glass jars, and stored in a desiccator.

Total nitrogen was determined by the macro-Kjeldahl procedure of Seales and Harrison,<sup>35</sup> and fat (ether-soluble) by a method based upon the procedure

### Placental Structure and Function

Structurally, the placenta is the tissue formed at the juncture of the vascular systems of the embryo and of the maternal organism. The closeness of this contact varies for different types of animals; it may be a very loose connection in which the barrier between the two blood circulations is quite substantial, such as the epitheliochorial type found in the horse and pig,<sup>17</sup> or the barrier may be a thin one by which the two circulations are closely bound, as in the hemochorial type found in man, monkeys, and the lower rodents.<sup>18</sup> The extensive contact between maternal and fetal circulations in man represents an area which has been estimated by Christoffersen<sup>19</sup> as between 10 and 13 square meters.

By the end of gestation the fetal portion of the human placenta has developed to such an extent that it forms the major part of the organ. In the process of growth the chorionic villi have burrowed deeply and interfused with the uterine tissue, where they are bathed in a pool of the mother's blood. Through their semipermeable covering, nutriments from the mother's blood are able to pass into the placental blood and be carried to the fetus, and excretory products are returned from fetus to mother. In all probability the villi do not act simply as mechanical filters, for as Corner<sup>20</sup> emphasizes, their covering is living tissue, and it may be able to act upon substances which pass through it, partially digesting them, or otherwise altering their chemical and physical nature.

The placenta, essentially an organ with a nutritional function, is well supplied with carbohydrate, protein, fat, enzymes, vitamins, hormones, and minerals. Though there is a dearth of information as to the progressive changes in the chemical composition of any one type of placenta, there can be no doubt that its chemical composition during gestation varies to suit the demands made upon it by the growing fetus. Szendi<sup>21</sup> has given evidence of a succession of peaks in the glycogen content, first in the maternal part of the placenta, then in the fetal part, then in the fetal lung, and lastly in the fetal liver. Hard, Reynolds, Orr, and Winbury<sup>22</sup> point out that placental carbohydrate and fat are reduced in the last quarter of pregnancy and it may well be that such changes in the placenta during development produce changes in its permeability and secretory activity. According to Zsigmond and Seipiadis,<sup>23</sup> the vitamin C content of the placenta increases during the course of pregnancy and then decreases near its termination. Another example of this changing content and permeability lies in the evidence that the rate of transfer of radioactive sodium across the placenta is very low in early pregnancy, but increases sixty-fold as gestation progresses, and then decreases somewhat at term.<sup>24</sup>

Besides acting as a supply depot, the human placenta seems to have a variety of other functions, among them that of being chief excretory organ of the fetus. As demonstrated by Brooksby and Newton<sup>25</sup> it also influences the water retention of the maternal organism. Upon the bursting of the amniotic sac and the destruction of the fetuses of pregnant mice about two-thirds of the way through gestation, they noted that the placenta was retained for some days and delivered at a time corresponding to normal full term. The animal did not return to its original weight until the placenta had been delivered, and this seemed to show that the placenta has the specific effect of giving rise to water retention. Needham<sup>26</sup> states: "In endocrinologic complexity, therefore, the placenta seems to outdo even the pituitary." Hormones similar to those of the anterior pituitary have been demonstrated<sup>27, 28</sup> and, since endocrine functions of the ovary are duplicated, the placenta may well be considered as an endocrine gland.



TABLE II. PROXIMATE COMPOSITION OF HUMAN PLACENTA

SUBJECT	WATER CONTENT*		DRY WEIGHT		TOTAL ASH			TOTAL ENERGY	
	GM.	PER CENT WET WT.	GM.	PER CENT WET WT.	GM.	PER CENT WET WT.	PER CENT DRY WT.	(CAL-ORIES)	PER GRAM DRY WT. (CAL-ORIES)
LF	564.7	85	96.3	15	7.6	1.1	7.8	510	5.3
VG	383.3	85	69.7	15	5.2	1.1	7.5	345	4.9
VK	281.8	86	45.2	14	3.4	1.0	7.4	237	5.2
VL	355.8	86	58.2	14	3.9	0.9	6.7	306	5.3
JM	502.0	85	90.0	15	11.6	2.0	12.9	443	4.9
DM	933.7	94	64.3	6	4.3	0.4	6.7	342	5.3
CO	654.6	92	58.4	8	3.6	0.5	6.1	309	5.3
VS	375.9	85	68.1	15	3.6	0.8	5.2	362	5.3
AS	546.0	85	96.0	15	16.0	2.5	16.6	451	4.7
Average	510.9	87	71.8	13	6.6	1.2	8.6	367	5.1

SUBJECT	TOTAL NITROGEN		TOTAL PROTEIN†			TOTAL FAT			PROTEIN TO FAT RATIO
	GM.	PER CENT DRY WT.	GM.	PER CENT WET WT.	PER CENT DRY WT.	GM.	PER CENT WET WT.	PER CENT DRY WT.	
LF	11.90	12	74	11	77	4.3	0.66	4.5	17
VG	8.47	12	53	12	76	2.7	0.59	3.8	20
VK	5.70	13	36	11	79	1.9	0.58	4.2	19
VL	7.27	12	45	11	78	2.4	0.57	4.1	19
JM	10.56	12	66	11	73	3.7	0.62	4.1	18
DM	8.06	12	50	5	78	2.4	0.24	3.7	21
CO	7.44	13	46	6	80	2.0	0.28	3.4	23
VS	8.64	13	54	12	79	2.8	0.62	4.1	19
AS	10.52	11	66	10	68	2.2	0.34	2.3	30
Average	8.73	12	55	10	77	2.7	0.50	3.8	20

\*Fresh or wet weight minus dry weight.

†Nitrogen multiplied by 6.25.

and testes of rats.<sup>39</sup> Other rat organs—liver, heart, lung, kidney, brain, muscle, and spleen—have higher percentages of total solids.<sup>39</sup> Soft organs of beef (heart, liver, kidney, brain, lung, stomach) and beef, veal, lamb, and pork muscle have lower water contents than does human placenta.<sup>40</sup> In fact, in water content the placenta more closely resembles such substances as milk or egg white. Its moisture content at term approximates that of a human fetus of about five and one-half months. Givens and Macy<sup>41</sup> have shown that the water content of the human fetus gradually decreases from 92 per cent at the third month to 72 per cent at birth. Individual organs do not necessarily show parallel changes in water content. According to Hard, Reynolds, and Winbury,<sup>22</sup> the guinea pig placenta is constant in its water content throughout gestation, fluctuating only +0.96 and -0.99 from a mean of 83.5 per cent. They found that the slight moisture decrease which occurred by the end of gestation was attributable to the maternal part only. In its high water content the placenta may seem to resemble an organism in an early stage of development. However, investigators<sup>42, 43</sup> have pointed out that the histologic and oxygen consumption studies of the human placenta during its development indicate that all of the morphologic and metabolic changes, which in the human body take a lifetime, occur in the placenta during the period of gestation. It is, then, at term an aged organ.

The average nitrogen content of the whole placenta was 8.73 Gm., a figure which approximates the nitrogen content of a 5- to 6-month-old fetus, i.e., 8.59 Gm.<sup>44</sup> The protein content of the placenta (nitrogen multiplied by 6.25) varied from 5 to 12 per cent of the fresh weight, averaging 10 per cent. Of the dry weight, with variations from 68 to 80 per cent, the average protein content was 77 per cent. On the wet weight basis, the content was far less than is found in most glandular organs and muscle,<sup>40</sup> but approximated the amounts found

given by Tidwell and Holt.<sup>35</sup> To obtain total ash values, after ether extraetion the sample was ashed overnight in a muffle furnace at 500° C. The Parr Oxygen Bomb Calorimeter was used to determine energy.<sup>35</sup>

### Results

During pregnancy the growth rate of the plaecenta does not parallel that of the fetus, since the former attains its maximum size early in gestation.<sup>11</sup> According to Wolfram<sup>36</sup> a definite ratio exists between the weight of the placenta and the weight of the fetus throughout the period of gestation. In the seventh month of pregnancy he found the ratio of fetal weight to placental weight to be 3.7 to 1, while at term it had increased to 7.5 to 1. Aberle, Morse, Thompson, and Pitney<sup>37</sup> studied 4,003 full-term births, male and female, and concluded that the correlation coefficients (+.506 for males and +.484 for females) showed that the weight of the placenta and the weight of the fetus influence each other to a large extent, but the fact that the correlation coefficient is not higher shows that other important influences must operate. For females they found the ratio of infant to placental weight to be 5.7 to 1, for males 5.8 to 1. For the placentas and full-term infants (all female except one) in this study the ratio was variable, ranging from 3.1 to 9.4, with an average of 6.5 to 1 (Table I).

TABLE I. RATIO OF INFANT BIRTH WEIGHT TO WEIGHT OF HUMAN PLACENTA

SUBJECT	BIRTH WEIGHT (GM.)	THIRD STAGE OF LABOR (MIN.)	PLACENTA FRESH WEIGHT (GM.)	RATIO OF BIRTH WEIGHT TO FRESH WEIGHT OF PLACENTA
LF	3,890	5	661	5.9 to 1
VG	3,720	4	453	8.2 to 1
VK	3,070	12	327	9.4 to 1
VL	3,500	2	414	8.4 to 1
JM	3,680	3	592	6.2 to 1
DM	3,070	4	998	3.1 to 1
CO	3,440	35	713	4.8 to 1
VS	3,230	10	444	7.3 to 1
AS	3,260	-	642	5.1 to 1
Average	3,429	-	583	6.5 to 1

The wet weights of the washed plaecentas (Table I) ranged from 327 to 998 Gm., with an average of 583 Gm. This variation was greater than that among the infant birth weights which ranged from 3,070 to 3,890 Gm. Largest birth weights were not indicative of larger plaecentas for the heaviest plaecenta, 998 Gm., came from the mother whose infant was the smallest. Aberle, Morse, Thompson, and Pitney<sup>37</sup> found a mean plaecental weight of 597 Gm. for female infants, 607 Gm. for males. They made no attempt to estimate the weight of placental tissue exclusive of blood, but weighed the plaecenta, eord, and membranes after removing blood clots with forceps, a proeedure which may account for their somewhat higher values.

The dried weights of the plaecentas showed less variation, although the highest dry weight, 96.3 Gm., was double the lowest, 45.2 Gm., the average being 71.8 Gm. (Table II). The dry substance averaged 13 per cent of the wet weight, and the average moisture content of 87 per cent, ranging from 85 to 94 per cent, shows the human plaecenta to be an organ relatively high in water, compared with glandular organs and musele. The per cent water content of placenta is similar to that given for testes, 84.5 per cent, by Taylor, Pollaek, and Williams,<sup>38</sup> but the other human tissues reported have lower moisture contents than plaecenta, notably the skin, 59 per cent, and adrenal glands, 61 per cent. The per cent dry weight of placenta is similar to that of the thymus

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in egg white.<sup>45</sup> Compared on the dry basis, the protein content agrees well with values for beef organs, and mammalian, avian, and crustacean muscle tissue.<sup>40</sup>

The fat content (ether-soluble) of the placenta is not high, varying from 0.24 to 0.66 per cent of the wet weight, and on a dry basis from 2.3 to 4.5 per cent, averaging 3.8 per cent. These values for ether-extractable material essentially represent the neutral or storage fat, and on the dry basis approximated, in general, the neutral fat content of rat and beef organs.<sup>46, 47</sup> According to Hard, Reynolds, and Winbury,<sup>22</sup> the fat content of the placenta is concentrated mainly in the fetal part.

In their protein to fat ratios, the placentas averaged 20 to 1, varying from 17 to 30. In the same approximate range of values fall the ratios of such tissues as beef brain, kidney, heart, lung, stomach, and lamb muscle.<sup>40, 47</sup>

The majority of the total ash values ranged from 5 to 8 per cent of the dry weight, which corresponds to values found for crustacean muscle and beef organs.<sup>39</sup> However, two placentas had ash contents of 13 and 17 per cent, respectively, making the average 8.6 per cent, which is somewhat higher than the amount in many animal tissues. Total ash per placenta averaged 6.6 Gm., which approximates the amount in a human embryo of five and one-half months.<sup>41</sup>

The energy value of the dried placenta was about 5 calories per gram, with a range of 4.7 to 5.3. This is approximately the caloric value of dried cow's milk,<sup>45</sup> and is slightly less than that for dried human milk.<sup>39</sup>

### Summary

From analyses of nine human placentas, values are given for wet weight, total solids, water content, nitrogen, protein (nitrogen multiplied by 6.25), fat (ether-soluble), ash, and energy. The water content was high and variable, averaging 87 per cent, while the dry weight averaged 13 per cent of the fresh weight. Protein averaged 77 per cent of the dry weight; fat, 3.8 per cent; and ash, 8.6 per cent. The average energy value of the placenta tissue was 5 calories per gram dry weight.

NOTE.—The second contribution on this subject, dealing with the lipid content of the placenta, will be included in the next issue.

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We feel that hypnoanalysis is a valuable adjunct to our therapeutic armamentarium because it effectively speeds up the diagnosis and obviates prolonged therapy. The technique of hypnoanalysis can be mastered by any physician who is familiar with the problems of psychodynamics and has a good understanding of psychological processes.

Many investigators acknowledge that the relief of psychogynecic conditions result from unintentional suggestions, *irrespective of the therapy used*. Since weak suggestion has been effective in bringing about cures, a type of psychotherapy utilizing modern and scientific suggestion and analysis as the main implement should be much more effective.

Pure hypnosis as described by the earlier investigators, Forel, Bernheim, Liebault, and Charcot, has been found wanting in many respects because only symptoms were removed. Hypnoanalysis, a combination of hypnosis and psychoanalysis, is a rational psychotherapeutic procedure. It is more effective because "insight" into the basic emotional difficulties responsible for the symptoms are recognized by the patient as the mechanism of cure.

Hypnoanalysis elicits underlying psychogenic and behavior disorders and enables the therapist and patient to ascertain the factors responsible for the symptom complex. It is used as a means of penetrating below the resistances of the patient and is helpful in integrating, synthesizing, and enforcing new and more wholesome attitudes. Also new personality patterns can be engrafted. Most important of all, it speeds up an ordinarily slow process.

### Technique of the Hypnoanalytical Method

A preliminary explanation of the nature of hypnosis is made, thereby correcting whatever misconceptions the patient may have. The hypnoanalytic method is a three-stage operation involving: first, conditioning and training in the phenomena of hypnosis, i.e., *rapport*, a condition in which the patient responds only to the therapist; *cataplexy* or muscular rigidity, during which the patient's normal capacities are enhanced; *amnesia*, the stage permitting the therapist to deal with painful memories without the patient's knowledge; *hyperamnesia*, or recall of memory and age *regression*; the following of *posthypnotic suggestions*; *somnambulism*, the "waking state of hypnosis;" second, free association, which consists of trains of thought arising spontaneously when restraints are removed; and last, reintegration of repressed material into consciousness. Hypnoanalysis, indeed, is mental surgery.

The following case histories are typical of our methods:

CASE 1.—Mrs. P. E., aged 36 years, para i, gravida ii; history of severe headaches since the age of ten, accompanied by photophobia, dizziness, nausea, and vomiting. Lower abdominal pain for sixteen years' duration. Palpitation, fatigue, nervousness, and suicidal tendencies, more marked during the past year.

Past medical history: Streptococcus infection of leg and sinusitis.

Surgical: Hymenectomy (1928) for dyspareunia and vaginismus. Brain operation (1932) for hemangioma.

Obstetric: Spontaneous delivery, 1932. Vaginal cesarean at 6½ months. Pregnancy terminated because of the headaches.

Gynecologic: Menses; onset at age of 15 years, "first period frightened her to death." irregular, dysmenorrhea occurred immediately after marriage (1928).

## THE TREATMENT OF PSYCHOGYNECIC DISORDERS BY HYPNOANALYSIS

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THE recent upsurge in psychosomatic medicine has given the profession a new understanding of old problems. It has shown that our division of medicine into specialties was arbitrary. In the multiple lights cast by psychosomatic investigations, the outline of once clear-cut clinical entities resolve themselves into component shadows. They do not fall in any one direction, but have the distressing habit of overshadowing several specialties.

This is forcefully demonstrated in functional gynecologic disorders, since it is obvious that these processes are the result of psychologic and physiologic factors. Psychogynecic derangements would therefore be a better term. The public is demanding help in this overlapping field. Therapy must be rapid, efficacious, and applicable to patients in all income groups.

Cooke<sup>1</sup> states, "Ninety-five per cent of the severity of human suffering is mental; a great deal of the symptomatology encountered in the practice of gynecies is of purely mental origin. Therefore, if we are to relieve the major part of our patients' suffering, we must do so through psychotherapy, and successful psychotherapy must be based upon an understanding of the patients' mental processes." The solution certainly will not be found in making the patient a traveling case history. Instead, the responsibility lies squarely with the gynecologist who is usually the first "specialist" to see the patient. The gynecologist can be of inestimable value in the field of prophylactic medicine because his contact with the disorder is early. Although psychogynecic disorders are of psychologic origin, and therefore in the field of the psychiatrist, he rarely sees the problem until it is far advanced and frequently incurable. Also, a thorough investigation of the emotional factors involved in psychogynecic complaints is impossible when there is too much division of authority.

A method which offers a relatively short and effective treatment when properly applied in functional gynecologic disorders is hypnoanalysis. Unfortunately, the preponderance of scientific work in this field is being done by psychologists for nonclinical investigation.

Hypnoanalysis has been used successfully to ameliorate many sensations of an unpleasant nature. It is known to be an effective and rapid form of therapy. At present it is being used extensively for the treatment of battle fatigue and other war neuroses. We agree with Brenman and Gill<sup>2</sup> who state, "Of all the methods of hypnotherapy, hypnoanalysis is the youngest and thus the least widely employed. It is our opinion, however, that it holds the greatest promise for a shortened method of psychotherapy." The skepticism and prejudice by the laity and profession are now diminishing in view of the increasing number of favorable reports.

realized that the headaches were due to her repressed hostility. They always occurred after intense emotional upsets. The lower abdominal pains, dysmenorrhea, and other psychosomatic symptoms were the "organ language" she used to verbalize for her neurosis; the frigidity. A complete change in this patient's personality occurred. All thoughts of suicide disappeared.

CASE 2.—Mrs. G. N., aged 22 years, para i, gravida i; history of lumbosacral backache and throbbing pain in left leg and knee. Past medical history was essentially negative. Patient stated that following the birth of her baby six weeks ago, she developed a pain in the lower part of her back. She had a rapid and painless two and one-half hour labor under nembutal analgesia. By the tenth day the backache was so severe she could not leave the hospital. Orthopedic consultation and x-rays of the lumbosacral spine were negative. The following therapy was instituted; opiates, physiotherapy, deep x-ray therapy, paravertebral procaine injections, direct infiltration of the sciatic nerve and traction. After six weeks of this treatment the patient still complained bitterly of pain in the back and left leg. Neurological consultation was negative. A tentative diagnosis of an intervertebral disc was made and a spinogram advised. Physical examination revealed a marked scoliosis due to considerable muscle spasm on the left side.

The constant unrelieved pain indicated a psychogenic origin. The patient was very intelligent and hypnoanalysis was advised. The first few sessions were devoted to conditioning her in hypnosis. Under somnambulism the patient was able to touch the floor without pain and the scoliosis and muscle spasm disappeared. Free association revealed that she expected to have the "pains of labor" which were absent during her confinement. Therefore, she felt she had missed something. After this session she felt much better. She was told not to consider herself cured until the basic emotional difficulties were resolved. During the next two hypnotic sessions she stated that her backache recurred when she saw her mother-in-law, and that she did not want to have this baby. When two months pregnant her former employer, whom she admired, died. This resulted in an attack of severe nausea and vomiting. This man was the antithesis of her husband with whom sexual relations had always been unsatisfactory. "Even though my husband, whom I love, is very considerate, I wish he would be more firm and masculine. My old boss was handsome, ambitious, meticulous, and just perfect in every way. I wanted to name my baby after him and my husband objected and became very angry. Perhaps if I probe a little deeper I will find the reason for my backache." This was an acknowledgment that an underlying unconscious conflict existed. She refused to believe that the baby belonged to her; also, the baby, being an intruder, would break up her marital relationship. She had not seen the baby since she left the hospital. She realized the backache would not clear up permanently until she consciously solved her conflict. She was left in a deep hypnotic state for three hours and told to review all the events leading up to the present. Amnesia for this session was induced. She was to reveal the results at the next session.

It was suggested that she leave her mother-in-law's home and return to her own home. Immediately on seeing her baby she began to vomit. The nausea and vomiting were so severe that she was hospitalized. Physical examination and a flat plate of the abdomen were negative. This vomiting was a rejection or "spitting at the unwanted baby." After three days of symptomatic therapy she left the hospital still complaining of her backache and walking with considerable difficulty. Scoliosis and muscle spasm were still present.

Deep hypnosis was instituted at the next session. She realized she had not been in love with her husband, but was actually in love with her dead employer.



Complete medical, gynecologic, and neurological examinations were negative for organic pathology. An electroencephalogram (1944) was within normal limits.

*Onset and Course.*—Patient states that her headaches began when she was 10 years old. Since then she consulted numerous physicians and clinics in America without obtaining relief. After a wide variety of symptomatic therapy, hypnosis was decided upon. The patient was hypnotized during a typical "migraine attack"; complete relief for the symptom was obtained. She was disassociated, and a specific amnesia produced for her true identity. The headaches always disappeared during the induction of this phenomenon of hypnosis. The patient tacitly acknowledged that the headaches, abdominal pain, and other symptoms might be on a neurotic basis, and hypnoanalysis was advised. The frigidity or symptom complex responsible for the above complaints was not mentioned at this time.

Hypnoanalytic therapy started with intensive training under hypnosis until the patient became a "somnambule." This "waking state" is the most suitable for psychotherapy. The technique and stages of hypnosis have been described by various investigators.<sup>3-5</sup> The best technique depends on the type of patient and personality of the therapist. All the stages of hypnosis are not always present in the same patient.

In the somnambulistic stage the patient was easily reverted to earlier periods of life. The information elicited concerning her early life ordinarily would have taken a much longer period under psychoanalysis. During this process of "age regression" harmful habit patterns, i.e., masturbation, faulty attitudes toward sex and pregnancy, personality disorders consisting of extreme hostility toward her parents, younger brother, husband, and daughter were discovered. Posthypnotic suggestions were given and followed and the patient was reorientated to her present chronologic age.

When she had successfully passed this phase, she was then prepared for the analytic, or second part of the hypnoanalysis. This consisted of free association which indicated her fear of disapproval and punishment by her father, her extremely sensitive nature, inadequate sexual knowledge, and lack of gratification. Free association became exceedingly easy once the resistances were disintegrated through hypnosis. Hence, orthodox psychoanalytic methods benefit from this simple effective spur. Her dreams were interpreted and handled as in an analysis. In addition, the dreams described in the hypnotic state were full of pertinent details, and their significance could be easily ascertained.

Now the patient was ready for the final phase. This involved the reintegration of material derived from the hypnotic sessions. It concerned the synthesizing and redistributing of the psychological processes formerly exploited by the symptom complex. During this final phase, posthypnotic suggestions were utilized to engraft new healthy attitudes toward sexual matters and the males in her family. She realized her unconscious hostility toward her father. She had feared him because he beat and criticized her from childhood and kept her ignorant of sex until her wedding night. This inadequate preparation for marriage also heightened the expectation of damage to her genitals and probably necessitated the hymenectomy. Her headaches began immediately after the brother entered the family constellation. He became her responsibility, and her father whipped her when anything happened to him. In contradistinction to her mental faculties and lack of attractiveness, the brother was brilliant and handsome. This produced additional early unconscious resentment toward males. The transition toward males was only partially accomplished by her marriage. The husband symbolized her father, causing further persistent unconscious anxieties regarding heterosexual activity. As a result of this "insight" the symptomatic meaning of her basic emotional problems became clearer. She



What is the value of psychotherapy which does not require conscious insight? How important is the matter of making the unconscious conscious? Erickson<sup>72</sup> reports two cases treated in which there is no history, no free association, no clear statements of the patient's problems, no transference, and yet a therapeutic result was achieved. Is symptomatic relief the criterion of successful psychotherapy? If the patient should be made aware of previously unknown unconscious strivings, is it necessary that she know all the steps through which her insight is achieved? More results must be evaluated before these questions are answered.

With the advent of hypnoanalysis, it no longer need defend itself against the charge that hypnosis is "nothing but suggestion." The methods described present a means of accomplishing vastly more in the way of psychogynecic rehabilitation than the older methods of symptomatic relief. This study points a way to research toward a therapy which may utilize all that has been learned by the gynecologist, hypnotherapist, and psychoanalyst.

### Frigidity

In taking up this symptom complex we must bear in mind that we are concerned with *true* frigidity, as differentiated from pseudofrigidity caused by ignorance and misconceptions about sexual matters, incorrect technique, or male impotence.

True frigidity may be defined as "the incapacity of women to have a vaginal orgasm."<sup>8</sup> Knight,<sup>9</sup> in his excellent article, states that "gynecologists and psychiatrists are aware that perhaps 75 per cent of all married women derive little or no pleasure from the sexual act, and that many not only experience no pleasure, but actually suffer revulsion and pain." This fact assumes added significance from a sociological and religious aspect because of increasing extramarital promiscuity and our high divorce rate.

Because enormous numbers of such cases are being seen by the inadequate number of psychiatrists and gynecologists, a more efficacious and rapid form of therapy is indicated. Current treatment involving hormone therapy (androgen),<sup>10, 11</sup> even if successful, is only substitutional. Surgery is valueless. Psychoanalysis, while successful, is expensive, time-consuming, and requires extensive technical training for the therapist. Since it is the gynecologist who, as sort of a father-confessor, treats the vast majority of functional gynecologic disturbances, many of psychological origin, a knowledge of psychopathology is as indispensable as histopathology. *He can and should be his own psychiatrist.*<sup>12</sup>

We feel that hypnoanalysis, a modification of hypnosis, is a rational and effective form of psychotherapy because less time and training are required. This modern and scientific method of therapy has been utilized in gynecology and obstetrics<sup>13-15</sup> and other branches of medicine. The experimental work of numerous investigators has shown that the objections to hypnosis as a therapeutic procedure can be eradicated by utilizing hypnoanalysis following the technique described above.

E. Bergler<sup>16</sup> maintains, "that a typical frigid woman does not suffer from a deficiency of libido, but from a neurosis." Hence, this form of therapy is ideal for the treatment of true frigidity, because every neurosis is an illness of

She wished that the latter could have been the father of the baby, and this accounted for her refusal to accept the child. She had never had an orgasm with her husband. She never complained of the frigidity because she did not know to whom to turn. She now realized that the backache was an alibi for her present unhappy marital status. Also it was foolish to be in love with a dead man. She decided a more healthy attitude toward her husband was possible.

The next few visits were devoted to integrating and synthesizing repressed material into her consciousness. This resulted in the acceptance of the baby, and for the first time in her life she experienced pleasure during intercourse. She felt that "a load had been taken off her back." Her backache completely disappeared and the symptom complex of frigidity had resolved itself. Up to Oct. 5, 1945, the patient has been very happy. Her unconscious conflict was too strong to be borne in consciousness, even when the patient knew what was troubling her.

### Discussion of the Hypnoanalytical Method

Lindner<sup>6</sup> states that, "hypnoanalysis can be described as an incisive approach which, more rapidly than other psychotherapeutic methods, cuts to the core of psychogenic and behavior disorders and enables the therapist to come to grips with the root causes in the dynamics of the disorder confronting him."

Under hypnoanalysis the patient's thoughts (free association) are spontaneous and unfold with ease. This freedom of behavior in a permissive atmosphere illustrates one of the most important aspects of hypnoanalysis. A wide latitude of expression is produced. The patient is not subservient, unconscious, or helpless. During age regression the patient's actions show the vividness with which she relives traumatic experiences. This "abreactive method" is a reliving of original experiences which takes place in her consciousness. The patient's recognition and reliving of old behavior patterns is the way she obtains "insight." She must understand the origin and the basis of her symptoms, how they are linked up with life's experiences, childhood pattern formations, and unnatural inhibitions. The symptom complex will disappear only when its symptomatic meaning has become clear to the patient.

The ego of the patient with its resistances and defenses is involved when hypnoanalysis is utilized, therefore the therapist has direct access to unconscious material. The insight gained is assimilated into the ego, and a significant change takes place. Hence, contrary to current Freudian opinion, the cure obtained through hypnoanalysis is *permanent*. No objection to the use of hypnoanalysis can be made because direct suggestion is not used.

The hypnotic technique is more rapid because the resistances are by-passed. It operates directly upon the conflict and, if solved, much of the defenses will spontaneously disappear. However, paradoxically this technique does not always require that the patient communicate or become aware of unconscious strivings. Consequently, two of our patients did not require that the unconscious be made conscious. They were able to find psychotherapeutic relief from symptoms without conscious exploration of the unconscious sources of their conflicts. Apparent recovery can take place in some patients with partial or even no insight.<sup>7</sup> The patient is only interested in recovery.

This classification excludes aplasias, hypoplasias, acquired organic lesions of the genitals, the consequences of destructive operations or accidents, incorrect technique, ignorance of sexual theories, and male impotence.

Excluded are the so-called "facultative" cases where the frigidity disappears and a normal orgasm is possible with certain men.

True frigidity on a purely psychic basis may be due to fear of punishment for violating sexual prohibitions. Again, frigidity may be due to conflicting loves, e.g., love of her father as opposed to love of her husband, love of herself as contrasted to love of her husband, and love of other women as opposed to love of men as represented by her husband. Uneconscious resentments and hates with reference to a wish for revenge on men, based on the "castration" complex, or a wish to avenge the mother for all the suffering she went through at the hands of the father may also lead to frigidity.

Included are many types in whom frigidity may be easily recognized and others in whom it is more overt—who use it as an escape, a flight from their own inadequacies. In this grouping we see the homosexuals, aggressive old maids, agitative female "champions" in constant competition with males, narcissists, and violent espousers of virginity. All of these types are presumptively frigid, and their frigidity includes no physical sex factor.

In our second classification we find a "contact factor" added to our psychic disturbance. Here we see the "gold digger," who is financially exploiting many sexual partners and husbands. The prostitute and the nymphomaniac, the latter in a fruitless search for satisfaction which is never achieved, belong to this group. The members of this class may make a partial adjustment and become involved in marriage. This solves the problem only outwardly. A closer inspection will demonstrate the same pattern of flight and combat interwoven with the marriage thread. The marital union may be characterized by refusal to assume any serious obligation of wifehood or motherhood. There is an excessive compensatory interest in card playing, club and sport pursuits, and a proportionate neglect of the husband. This type will take great interest in traveling alone, purchasing expensive clothes, perhaps even the aggressive pursuit of a career. Pregnancy is avoided as a nuisance, or even a calamity.

Swinging the pendulum the other way but still within the arc of our second group, we observe those women who carry out their wifely duties with overwhelming vigor—also as an escape, and also to the exclusion of the husband. They have complete absorption in the household to the point of obsessional cleanliness and orderliness. There may be a flurry of glorified motherhood, resulting in numerous children conceived with indifference and lack of pleasure, on whom there is bestowed a surprising excess of attention and solicitude; the husband, as always, being relegated to the background. They must assume a lifetime of martyrdom, resignation, and suffering; an adoption of extreme prudishness is also not common, so that nothing but frigidity can result.

In this second grouping the physical factor is definite and demonstrable. There is no relationship between the type and degrees of frigidity and the sensitivity of the vagina.

the unconsciousness. These women actually are attending a psychological masquerade, using the symptoms as a pretext for obtaining no pleasure from sexual intercourse. Nearly all of our cases presented themselves with complaints of dysmenorrhea, pelvic pain, backache, migraine headaches, and a host of other symptoms as an alibi for their lack of sexual gratification. Some of our patients had not one, but two abdominal operations without relief of the original complaint.

### Psychogynecic Causes for Frigidity

Greenhill<sup>17</sup> states, "that the psychosexual factors in feminine development actually involves two organs, that the clitoris plays the dominant role in childhood." This is the most easily discovered part of the female genitalia and the one which yields the most pleasure when stimulated. Therefore, all the attention is focused upon the clitoris. This leads to suppression of the awareness of the vagina. The lack of normal pleasurable vaginal sensitivity to stimulation may be due to the denial of the vagina and the effect of pleasure seeking on the clitoris. Greenhill<sup>17</sup> further states, "the other organ is the vagina, which is psychologically unimportant until puberty. In the child, the clitoris gives sexual satisfaction, while in the normal adult woman the vagina is the principal sexual organ. In frigid women, however, the transference of sexual satisfaction and excitement from the clitoris to the vagina does not take place. Hence, such women possess an infantile erotic zone, and not the adult one."

Knight<sup>18</sup> states that the dynamics of this neurosis has its core in the little girl's reaction to the discovery that she is lacking in an external sexual organ possessed by the little boy, so she believes that she, too, must have once had a penis of which she was punitively deprived by the parents, or that she will somehow be given one or will grow one later. Fears, envies, and resentments proceed from the shock of this discovery, and initiate the development of conflicting hate and love toward parents, siblings, and other significant persons. Distorted sexual theories and neurotic attitudes, symptoms and personality traits derive from this source. His excellent recommendations should be followed by physicians.

All investigators agree that these reactions of envy of men and fear of damage to the genitals play at least some part in the psychology of every girl, and that in many cases they are the dominating factors in personality development. Since most of the fears of mutilation, menstrual suffering, and hostile envious feelings toward men are unconscious and not to be elicited by ordinary interrogation or observations of outward behavior, we have chosen this ordinary refractory condition for treatment by hypnoanalysis.

### Classification of Frigidity

The Menninger<sup>19</sup> classification based on the varieties of frigidity, and Hitschman's and Bergler's<sup>8</sup> based on the degree of pleasurable sensitivity in the genitals ranging from great aversion and painful submission down to frigidity of the nymphomania type are excellent. Also the Rado<sup>20</sup> modification based on reactions to sexual anxiety were taken into consideration.

For purposes of simplicity we have resolved the above groupings into two subdivisions.

- A. True frigidity, founded on purely psychic mechanisms.
- B. True frigidity, founded on psychophysical mechanism.

4. It is an illness of the unconscious; a neurosis.
5. Other gynecologic "symptom-equivalents" mask this "organ neurosis."
6. Because of the universality of this symptom, and to obviate the division of authority, every gynecologist must be his own psychiatrist.
7. Comprehension of the psychodynamics of this symptom complex (true frigidity) must be understood.
8. Hypnoanalysis is a rational procedure in psychogynecic therapy because the recovered material is replete with significant details, new personality patterns can be engrafted, symptom-removal by direct suggestion is not utilized, and the cures, even when spontaneous, are complete and permanent.
9. Hypnoanalysis and its associative phenomena of age regression, recall of memory, free association, and posthypnotic suggestion are tremendous time-savers.
10. Hypnoanalysis varies only in degree from psychoanalysis, since it utilizes many of the concepts of the Freudian theory, i.e., interpretation of the transference, free association, piece-meal disintegration of the patient's resistances, reintegration into consciousness (assimilation by the ego) of the repressed material, and the redistribution of the psychological energies formerly exploited by the symptom complex of frigidity. Thus the patient gains insight into factors responsible for the symptom complex.
11. The technique of hypnoanalysis can be mastered by any physician who understands the psychological processes of present-day psychopathology.
12. A current review of the accepted factors responsible for the symptom complex of frigidity is presented.

The author is particularly indebted to Dr. J. P. Greenhill and Dr. S. F. Wollen for their valuable aid.

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Vaginal sensitivity may vary from complete anesthesia to exquisite receptivity. The personal attitude may range from complete revulsion, disgust, and the desire to get it over with in a hurry, to a strong sense of excitement, mounting repeatedly, but with no organismic climax and, hence, the hope for contact of long duration. The vaginal secretion may be absent, scanty, or voluminous. There may or may not be a clitoric orgasm, but never a true vaginal orgasm.

All of these possibilities, or a combination of any of them, occurs in frigid women. They can occur in women with vaginismus and dyspareunia.

### Hypnoanalysis in Frigidity

It is our contention that for the common gynecologic disorder of frigidity, hypnoanalysis is a rapid and rational form of therapy. First, because it is an illness of the unconscious (a neurosis) and not amenable to routine therapy. Second, it is masked by other symptom-equivalents, elicited only after extensive diagnostic procedures. If we are fully aware of the psychosomatic implications, if we discern the intricate psychic ramifications, how can we in all sincerity continue to treat these conditions with surgery and endocrine substitutional therapy alone? How can we approve the tediousness of classical psychoanalysis in a problem which cries out for relatively rapid relief?

Of all psychogynecic problems, none has demonstrated the efficacy and rapidity of hypnoanalysis more forcefully than the common complaint of frigidity.

### Results

Nine out of twelve cases of true frigidity, after a wide variety of symptomatic treatment, were permanently relieved utilizing this method. There were three failures in our limited series of cases. One patient was found to be a latent homosexual. It was decided not to attempt inversion in this case. Two other patients were not relieved following fifteen and twenty-five hours of therapy, respectively.

Two patients were permanently relieved spontaneously without any manifest reasons being revealed to the therapist. This may be due to the fact that the unconscious was made conscious of the extrapsychic conflict.

The shortest amount of time necessary to cure this symptom complex was eight hours, while the longest was sixty hours. We believe this is one of the first reports on frigidity in the American literature successfully treated by hypnoanalysis. This promising method offers a fertile field for investigators and should be evaluated by others for the ultimate welfare of psychogynecic patients of the future.

### Conclusions

1. The specialties of gynecology and psychiatry overlap. Latent psychological factors (the psyche) are as responsible as the reproductive organs for many functional gynecologic conditions.

2. The vast majority of patients, especially in functional gynecologic disorders, are likely to present some psychological cause for their physiologically expressed disturbances.

3. True frigidity is a common problem in gynecology.

positive correlation between breech presentations and contracted pelves, or other conditions which might prevent engagement of the fetal head.

Vartan<sup>4, 5</sup> and Stein<sup>6</sup> have made similar observations regarding the negligible importance of deformities of the maternal pelvis in causing breech presentations. Vartan, for example, found disproportion in only 1.3 per cent of his cases. Moreover, since placenta previa occurred in only 3.2 per cent of his cases, he concludes that it cannot be considered an important etiological factor.

Westman<sup>7</sup> found that among 993 breech deliveries at the Stockholm University Woman's Clinic, contracted pelves, abnormalities of the uterus, and polyhydramnios were not significant factors. Goethals<sup>8</sup> found that placenta previa and abruptio placenta were respectively three and five times more often associated with breech presentations than with occipital. It would seem, however, that the fact that both of these conditions are frequently seen among premature infants, where breech presentation occurs very commonly, tends to minimize the possibility of causal association.

In an analysis of 793 cases of breech delivery, Newell<sup>9</sup> reports that 17, or 2.2 per cent, of the mothers had previously been delivered of a breech. In only 6 per cent of his series could he find any association with factors reputed to predispose to breech presentation. Only 34 (4.2 per cent) of the 793 breech presentations in Newell's series were seen among women with contracted pelves.

*B. Transverse Presentations.*—From a mechanical standpoint, transverse presentations are quite analogous to breech presentations, the error in polarity being merely one of degree.

In general, the same factors which are claimed to cause breech presentations are also assumed to operate in the production of transverse presentations. Thus, Novey and Schneider<sup>10</sup> feel that factors which prevent engagement of the fetal head in the pelvis or allow unusual mobility on the part of the fetus are responsible for the majority of such presentations.

While I hope to prove that these authors are mistaken in their major premises, I do feel that they are quite right in another of their suggestions—that pure accident also plays a role. As they point out, a shoulder will frequently fix in the pelvis should membranes rupture at a time when the fetus has not yet completed spontaneous cephalic version.

*C. Face and persistent brow presentations.*—Posner and Buch<sup>11</sup> studied 79 cases of face and persistent brow presentations and found what they believed to be an etiologic factor in 63.5 per cent. Their list, with the additions of cord entanglements and fetuses weighing over 8.5 pounds, is essentially the same as that already given for breeches.

Jungman,<sup>12</sup> on the other hand, from a study of ten cases of deflexion attitudes, believes that the condition is due entirely to the shape of the fetal head, the occiput in such cases being unusually long in relation to the sinciput.

### Materials and Data

From the records of fetal and neonatal necropsies performed at the Chicago Lying-in Hospital and from a smaller group performed at the Minneapolis General Hospital under the supervision of Dr. Fred L. Adair, I have collected 1,705 cases of congenitally malformed fetuses and infants weighing over 400 Gm.\*

Information concerning the type of presentation was available in 1,471 (86.3 per cent) of these cases. In all of the cases autopsy was complete and included routine microscopic tissue examinations as well as special examinations where the latter were indicated.

\*The weight above which, by Illinois law, a stillbirth or death certificate is required.

# ABNORMAL PRESENTATIONS AMONG MALFORMED INFANTS

## With Suggestions Concerning the Etiology

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**C**ONGENITAL malformations of the fetus are well known to predispose to abnormal presentations.<sup>1, 2</sup> The usual explanation given for this phenomenon is that fetal deformities interfere with the normal process of accommodation between the fetal head and the maternal pelvis.

I have recently been studying, at the Chicago Lying-in Hospital, a series of 1,705 malformed fetuses and infants, a series of sufficient size to give statistical significance to many of the findings regarding smaller subgroups within it. In the hope of contributing to the study of abnormal presentations, I have reviewed the manner in which these fetuses presented.

In the light of these findings, I propose to re-examine here the importance of malformations as an etiologic factor in abnormal presentations. I hope, further, to demonstrate certain fallacies which underlie many of the older ideas regarding the etiology of breech presentations, as well as to correlate my findings with newer theories regarding the causes of such presentations.

### Review of Alleged Etiologic Factors

Many etiologic factors are known or assumed to play a part in determining the presentation of the fetus. The flexed head, at least in fetuses at or near term, is generally acknowledged to be the normal presenting part, if for no other reasons than because of the frequency with which this attitude and presentation occur, and because of the relative ease and safety with which the majority of fetuses presenting in this manner are delivered.

Cephalic presentation is assumed to be the result of the process of accommodation between a normal pelvis, a normal uterus, and a normal term fetus.

Concerning the less commonly encountered presentations—breech, transverse, and cephalic attitudes of deflexion—there is no unanimity of opinion. Among the many factors which are claimed, justly or unjustly, to predispose to such presentations are abnormalities of the bony pelvis or soft parts, pelvic or uterine tumors, uterine anomalies, gravity, polyhydramnios, multiple pregnancy, prematurity, abnormal locations of the placenta, abruptio placenta, multiparity, advancing maternal age, hereditary predisposition, and maceration and malformations of the fetus.

In recent years, many of these alleged factors have been re-examined and the significance of a number of them has been laid open to considerable question.

**A. Breech Presentations.**—For example, Moore and Steptoe<sup>3</sup> studied the records of 1,444 cases of primary breech delivery at Johns Hopkins Hospital and found that, contrary to the usual textbook statements, the only factors of apparent significance in the production of breech presentations were prematurity, placenta previa, and malformations of the fetus. They were unable to find a



## Results

Of the 1,471 cases, 257, or 17.5 per cent, of malformed infants were delivered from presentations other than the occipital. (The face and brow presentations which occurred among the 220 anencephalic and iniencephalic monsters have been excluded from these calculations, because the nature of these malformations makes such presentations more closely "normal" than the occipital would be.) Among the control group, presentations other than occipital occurred in 4.4 per cent of the cases.

Thus, breech presentations, transverse presentations, and cephalic attitudes of deflexion occurred four times as often among malformed fetuses weighing over 400 Gm. as they did among 17,728 consecutive deliveries (which included fetuses of all weights over 400 Gm., as well as over 150 malformed fetuses which were delivered among that series).

In the malformed series, 834 infants weighed 2,500 Gm. or more. In this group, presentations other than occipital occurred in 22.7 per cent (as against 17.5 per cent for all of the malformed group). Among that fraction of the control group which weighed 2,500 Gm. or more, 3.3 per cent presented by a part other than the occiput. Thus, the series of larger malformed infants presented abnormally approximately seven times as often as did the control group of the larger babies.

Since malformed fetuses as a group often weigh less than normal fetuses of the same intrauterine age, it has been suggested that the smaller size of the malformed fetuses is really the determining factor in the increased incidence of breech presentations seen among them, rather than the malformations themselves. The proponents of this theory argue that so far as being a determinant in the type of presentation, malformations thus have the same status as prematurity.

The statistics which I have presented disprove this idea entirely. When malformed fetuses are large enough so that fetal weight becomes in every case a significant factor, the malformations in some way cause seven times more abnormal presentations than would be expected from chance alone.

### Malformations in Relation to Other Possible Etiologic Factors

Pressed to explain this unusual frequency, textbook authors patiently point out that the breech of an anencephalic or hydrocephalic monster accommodates more easily to the maternal pelvis than does its head (but what of the many malformed fetuses without cranial defects who present as breeches?); or, that the associated polyhydramnios keeps the fetus free-floating (yet polyhydramnios is by no means the constant accompaniment of malformed fetuses); or, that the relatively small size of most monsters accomplishes the same thing (but many malformed fetuses weigh as much or more than normal term fetuses). Moreover, it would seem reasonable that if disproportion due to the head-size of a hydrocephalic monster causes breech presentation, anencephalic monsters would never present as breeches. But this is by no means the case.

In the present study an attempt has been made to find some sort of common denominator which would explain the unusual frequency of abnormal presentations, if not in all, at least among the majority of malformed fetuses. As a part of this, I have reviewed the frequency with which various other factors alleged to produce breech and transverse presentations occurred in the present series,

Certain minor anomalies, e.g., accessory lobulations of organs, were not considered of sufficient importance to warrant inclusion in the series. In a communication now in preparation,<sup>13</sup> the incidence of the various malformations will be presented in detail. Because of the frequency with which multiple malformations occur in the same infant, the classification of malformations has necessarily been an arbitrary one. Malformations have been divided into "major" and "minor" headings, depending usually upon whether or not the anomaly is incompatible with prolonged life. Where two or more major malformations occurred in the same infant, the case has been classified under the organ system where the most gross malformation occurred. Thus, an anencephalic monster with polydactylia would be classified under "Central Nervous System," whereas an infant with gastroschisis and a major malformation of the heart would be classed under "Gastrointestinal."

Table I summarizes the method of presentation of these 1,471 malformed fetuses and infants, arranged according to the chief malformation. For comparison, data is appended concerning the presentation of all infants (17,728) delivered at the Chicago Lying-in Hospital from May, 1931, to January, 1938.<sup>14</sup>

TABLE I. ABNORMAL METHODS OF PRESENTATION AMONG 1,471 MALFORMED INFANTS BY PERCENTAGES, ARRANGED ACCORDING TO WEIGHTS

MALFORMATION	TOTAL CASES	CASES OVER 2,500 GM.		PRESENTATION						TOTALS	
				BREECH		FACE AND BROW		TRANSVERSE			
		NUM-BER	PER CENT	ALL CASES	OVER 2,500 GM.	ALL CASES	OVER 2,500 GM.	ALL CASES	OVER 2,500 GM.	ALL CASES	OVER 2,500 GM.
<i>Central Nervous System</i>	589	298	50.6	20.5	29.8	1.9	1.7	1.0	2.0	22.5	33.6
Hydrocephalus	265	177	66.8	24.9	32.7	2.3	2.2	0.7	1.1	27.9	36.1
Anencephalus	220	61	27.7	17.0	27.8	*	*	1.4	4.9	*	*
Mongolism	40	30	75.0	10.0	6.7	2.5	3.3	0.0	0.0	12.5	10.0
Spinal rachischisis	63	29	46.0	22.3	37.9	0.0	0.0	1.5	3.4	23.8	41.4
Miscellaneous	1	1	100.0	0.0	100.0	0.0	0.0	0.0	0.0	0.0	100.0
<i>Cardiovascular</i>	297	200	67.3	7.4	8.5	0.7	1.0	0.3	0.5	8.4	10.0
<i>Gastrointestinal</i>	173	115	66.5	13.3	12.2	0.0	0.0	0.6	0.9	13.9	13.1
<i>Respiratory</i>	18	8	44.4	33.3	50.0	0.0	0.0	0.0	0.0	33.3	50.0
<i>Skeletal</i>	184	93	50.5	14.1	16.1	1.1	2.1	0.5	1.0	15.7	19.3
Achondroplasia	13	7	53.8	38.5	71.4	15.4	28.6	0.0	0.0	53.9	100.0
Extremities	51	16	31.4	17.6	18.7	0.0	0.0	2.0	6.3	19.6	25.0
Herniations	78	46	59.0	2.5	0.0	0.0	0.0	0.0	0.0	2.5	0.0
Miscellaneous	42	24	57.1	23.8	29.1	0.0	0.0	0.0	0.0	23.8	29.1
<i>Urinary</i>	141	78	55.3	23.4	33.3	0.0	0.0	0.8	1.3	24.2	34.6
Kidney	107	59	55.1	26.1	37.3	0.0	0.0	0.9	1.7	27.1	39.0
Miscellaneous	34	19	55.8	14.7	21.0	0.0	0.0	0.0	0.0	14.7	21.0
<i>Tumors</i>	39	27	69.0	7.7	11.1	0.0	0.0	0.0	0.0	7.7	11.1
<i>Miscellaneous</i>	30	15	50.0	10.0	13.3	0.0	0.0	0.0	0.0	10.0	13.3
<i>Total</i>	1,471	834	56.7	16.1	20.4	0.7	1.1	0.7	1.2	17.5	22.7
<i>Chicago Lying-in Group†</i>	17,728			4.0	3.0	0.2	0.2-	0.2	0.2-	4.4	3.3

\*Not included in calculations (see text).

†17,728 consecutive deliveries at the Chicago Lying-in Hospital are appended for comparison.

Waters<sup>15</sup> and others have called attention to the necessity, until recently unheeded, of differentiating between the premature, nonfixed fetus and the term fetus. In the former group, for example, breech presentation is considered by some authors to be normal; at any rate, fetal size can hardly be considered a factor of significance in determining presentation. For this reason I have studied my data not only in regard to the total series of malformed infants, but also to that fraction of the series weighing 2,500 Gm. or more.

and intestines. And, except for the group of achondroplasties, all of these groups presented less often as breeches than did the series as a whole. Thus I feel that multiparity, with its relaxation of the maternal soft parts and abdominal wall, is hardly a factor, for I plan to present below what seems to me to be an adequate explanation for the frequent occurrence of breech presentations in achondroplasia. Nor is advancing maternal age a factor, except in achondroplasia and mongolism.

Abruptio placenta occurred in 32 cases (2.2 per cent)—again, not frequently enough to explain many abnormal presentations.

Information is not available regarding the methods of delivery of the siblings of this series. No statement can be made, therefore, regarding a possible hereditary predisposition to breech presentation. But, regardless of the fact that breech presentations have recurred in the same mother from three to nine times,<sup>18</sup> recurrences are by no means the rule, and hereditary predisposition explains few abnormal presentations.

In addition to considering the above factors, I have also reviewed these cases with the possibility in mind that abnormal presentations might produce congenital malformations, rather than vice versa. Chapple and Davidson<sup>19</sup> have shown that in some instances of skeletal—and especially hip—deformities, this actually occurs. I have been unable, however, to find even a possible relationship of this kind in an appreciable number of cases.

### Comment

I believe that I have demonstrated beyond reasonable doubt that something inherent in malformed fetuses causes frequent abnormal presentations. The explanations which are usually given for this association have been reviewed and the fallacious reasoning behind them has been pointed out. Moreover why, if the explanation were merely one of cephalopelvic disproportion, would nearly two-thirds of the hydrocephalic group weighing over 2,500 Gm.—where surely the influence of cephalopelvic disproportion would be at its greatest—present normally?

I believe that the answer to this question is to be found in the excellent but not widely known work of Vartan<sup>4, 5</sup> and Stein.<sup>6</sup> After close studies of large series of breech presentations among normal infants, they have independently arrived at the conclusion that fetal attitudes of deflexion (not only of the head, but also of the extremities) are of primary importance in predisposing to breech and transverse presentations.

Thus, they assign to the fetus an active role in helping to determine its own presentation, rather than the purely passive one which it is usually considered to play. A careful study of the work of these investigators cannot help but impress the reader with the logic and reasonableness of their beliefs.

It is well known, for example, that the commonest variety of breech presentation is with the legs extended. Frank breeches have been reported in from 47 to over 80 per cent of all such presentations; complete breeches, in from 3 to 6 per cent.<sup>20-24</sup>

Vartan considers that in breech presentations the fetus ordinarily tends to undergo spontaneous version as term approaches, and that persistent breech presentations result from the presence of some factor which prevents spontane-

TABLE II. OBSTETRIC COMPLICATIONS REPORTED AMONG THE MOTHERS OF 1,471 CONGENITALLY MALFORMED INFANTS, WHICH ARE ALLEGED TO CAUSE BREECH PRESENTATIONS

	CASES	PER CENT
Abruptio placenta	32	2.2
Multiple pregnancy	47	3.2
Pelvic and uterine tumors	16	1.1
Pelvic deformities (bony)	69	4.7
Placenta previa	34	2.3
Polyhydramnios	105	7.2
Uterine anomalies	15	1.1

having in mind the possibility that a malformation of the fetus might be merely the incidental accompaniment of a more significant etiologic factor (Table II).

Contractions of the maternal pelvis were seen with less than usual frequency (4.7 per cent). This is hardly surprising for, as Vartan<sup>5</sup> points out, the ultimate position of the fetus is in most cases decided long before the fetus makes any real attempt to enter the pelvic brim. Thus pelvic deformities can hardly be expected to play an important part in causing breech presentations.

Pelvic and uterine tumors of significant size were unusual (1.1 per cent), as were uterine anomalies (1.1 per cent).

Polyhydramnios was recorded in only 105 cases (7.2 per cent). This finding is in agreement with other recent reports which demonstrate that polyhydramnios is only occasionally seen with fetal deformities.

There were 47 twins in this series, of whom eight comprised four pairs showing malformations. This is an incidence of one in 39.5 pregnancies, or 2.2 times the expected frequency. But while multiple pregnancy is unquestionably a factor in causing breech presentations (and incidentally is quite probably a factor in the etiology of malformations<sup>16</sup>), twinning did not occur frequently enough to explain more than a few of the breech presentations.

Attention has already been called to the fact that prematurity—or at least fetal size—is definitely a factor predisposing to abnormal presentations. That it is a factor independent of the malformations is seen by referring to Table I. In the larger malformed fetuses where prematurity does not operate, the loss of this factor favoring abnormal presentations is more than compensated for by the presence of the malformation itself.

Placenta previa occurred in 34 cases (2.3 per cent). While this is of interest in verifying the work of Greenhill<sup>17</sup> regarding the frequent association of monsters with this condition, it still occurred too infrequently to be considered a potent factor.

Nor will the so-called "gravity theory" suffice. This convenient explanation for the preponderance of cephalic presentations holds that since the normal term fetal head is heavier than the breech, it assumes a dependent position because of gravity. However, the normal premature fetal head is relatively much heavier than the breech, but breech positions are exceedingly common during those periods of gestation. Moreover, were this theory correct, hydrocephalic monsters would never present as breeches. And yet they do so nearly one-third of the time.

Multiparity, despite the contention of a few investigators, is not a significant factor in the production of malformations. Indeed, there was a slight but definite tendency toward primogeniture in all malformations except a few of the smaller groups. The tendency toward multiparity was seen only in achondroplasia, mongolism, and in infants with anomalies of the gall bladder

fetuses with spinal rachischisis are invariably extended to some degree, the rachischisis splinting the spine and preventing its normal flexion. Moreover, liveborn infants with serious malformations of the spinal cord and the central nervous system nearly always present motor dysfunctions of various sorts, frequently of the neck and extremities. In spinal rachischisis, dysfunctions of the lower extremities are extremely common. I believe that such neurologic lesions are of great importance in causing deflexion attitudes because the motor difficulty which fetuses with these anomalies have prevents or makes difficult their assuming the normal fetal attitude of flexion.

The military attitude of deflexion is a constant characteristic of achondroplasia. Since 1909, when Das<sup>28</sup> made his first report on the subject, the association of this condition with deflexion attitudes and dystocia has been recognized.

It is felt that the frequency with which fetuses with urinary tract anomalies—notably polycystic kidneys—present abnormally is on a basis of their abdominal enlargement. It seems quite apparent that normal flexion of the fetal spine and flexion of the extremities upon the trunk would be effectively prevented. This is borne out by the frequency of breech presentations among a number of groups which have not been listed in Table I because of their small size—notably gastrorachischisis, intra-abdominal tumors, and other enlargements of the trunk.

### Summary

1. The methods of presentation of 1,471 congenitally malformed fetuses weighing over 400 Gm. have been reviewed. They are compared with the presentations of all infants weighing over 400 Gm. which were delivered at the Chicago Lying-in Hospital over a 6½-year period.

2. Among the malformed group, breech, transverse, and face and brow presentations occurred four times as often as they did among the "control group."

3. Among malformed fetuses weighing 2,500 Gm. or more, breech, transverse, and face and brow presentations were seen approximately seven times as often as they occurred among that portion of the "control group" which weighed 2,500 Gm. or more.

4. In an attempt to learn the reason for the many abnormal presentations among malformed fetuses, the factors claimed to be of etiologic importance in the production of abnormal presentations are reviewed. Most critical studies in the recent literature agree that of these many factors, only prematurity and fetal malformations occur often enough to explain more than a very few abnormal presentations.

5. The relationships of the alleged factors to fetal malformations have been studied and their significance is shown to be either nonexistent or very slight.

6. Deflexion attitudes have been shown to occur very frequently among malformed fetuses. They have also been reported to occur in over 80 per cent of all breech presentations among normal fetuses.

7. Evidence is presented which suggests that in the various groups of malformed fetuses which present abnormally with the greatest frequency, the

ous version from occurring. In his own series of 969 breech deliveries, he found that in 37.3 per cent, extension of the legs occurred; in 32.7 per cent, multiple pregnancy and prematurity; and, in only 4.5 per cent, placenta previa and/or a contracted pelvis.

Stein calls attention to the relative infrequency of deflexed attitudes among cephalic presentations, but to their high frequency in other presentations. By x-ray studies, he has demonstrated not only the frequency of extended positions among breeches—frank and footlings (for single and double footlings are also positions of partial extension)—but also the other evidences of deflexion. The spine, for example, is frequently straightened. The head is often turned to one side or is erect, as in military attitude. One or both arms are frequently extended.

Stein's description of the various characteristic breech attitudes of deflexion is borne out by what little other roentgenographic work has been done on this subject, notably that of Warnekros.<sup>25</sup>

That breech attitudes of deflexion hinder spontaneous cephalic version is well known. Ryder<sup>26</sup> found that, at least in primiparas, next to postponing attempts at external cephalic version until too late in pregnancy, the most common cause of failure of the attempted version is extended legs of the fetus. Donovan<sup>27</sup> has also commented upon this. Siegel and McNally<sup>23</sup> feel that the presence of a frank breech is a definite contraindication to attempts at external version. The extended legs, they point out, splint the body so that the baby cannot be made to flex sufficiently to make version easy: a compound presentation may result from the attempt.

If, as I am convinced, deflexion is a factor in causing breech presentations at term, the frequency of incomplete, or deflexed, breeches makes deflexion attitudes far and away the most important factor in the production of breech births. Stein has found deflexion attitudes in over 50 per cent of his series of breeches. As noted above, other authors report deflexion attitudes in over 80 per cent of their breech deliveries.

The present series of malformed fetuses has been reviewed with the work of Stein and Vartan in mind. I believe that their premise comes closest to being a common denominator in explaining the unusual frequency with which the many apparently unrelated groups of malformed fetuses present abnormally.

Unfortunately, roentgenographic studies of statistically significant groups of malformed fetuses have not been carried out. I believe, however, that my conclusions are almost equally well supported on the basis of clinical observation.

Breech and other abnormal deliveries are seen most often (Table I) in the following malformed groups: hydrocephalus, anencephalus, spinal rachischisis, achondroplasia, and in anomalies of the respiratory and urinary systems.

A deflexed attitude of the hydrocephalic head is common. The heads of anencephalics are similarly held in extension; indeed, the nature of the anomaly makes normal flexion of the neck and head impossible. The spinal columns of

# HIGH PROTEIN, LOW CALORIC DIET FOR THE PREVENTION OF TOXEMIA OF PREGNANCY

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UNTIL recently, little progress has been reported in the prophylaxis of that most formidable, and as yet poorly understood, enemy of the child-bearing woman, toxemia of pregnancy. Nevertheless, it is my conviction that the number of potential toxemic patients can be vastly reduced, if not entirely eliminated, by adequate prenatal care.

The report presented here covers the observation of 1,000 pregnant women, and the results obtained by a regime of rigid weight control without interfering with adequate nutrition. The immediate objective was a restriction of the total increase of weight to 16 pounds or less during pregnancy, and a maximum of 2 pounds in any one month. The results, it is believed, proved well worth the effort put forth by both the patients and the physician.

All of the patients were within normal weight range when first seen. Weight at the time of conception was accepted as normal if it was within 10 pounds of the following weight, height, and age chart:

Height	Ages 16 to 26		
	Weight		
60 inches	106	pounds	A 10-pound variation was allowed for variation in physique
61 inches	108	pounds	
62 inches	110½	pounds	
63 inches	113	pounds	
64 inches	117	pounds	
65 inches	120	pounds	An additional pound was allowed for each year over 26
66 inches	123½	pounds	
67 inches	127	pounds	
68 inches	131	pounds	
69 inches	134½	pounds	

All the patients included were organically sound as far as could be determined. Patients with initial blood pressures over 130 systolic and 80 diastolic were considered abnormal, and are not included in the group.

Cardiac, pulmonary, and mental disease can be determined quite accurately prior to conception or early in pregnancy, but the hepatic and renal reserve cannot be satisfactorily estimated as possible complications of pregnancy. Dieckmann<sup>1</sup> enumerates 36 tests for kidney function, and states that it would not be possible to determine the true renal reserve, even if all these tests were employed. Likewise, the relation of the endocrine glands to toxemia is not clear. Thus, it is impossible to make an accurate prediction of a woman's capacity for childbearing, and it would therefore seem logical to assume that every gravida is at least a potential candidate for toxemia of pregnancy.

Successful results from this dietary regime depend on two factors: first, the patient must be made to understand the purpose of the diet; second, the doctor

malformations have caused a deflexion attitude. It is felt that this factor explains more satisfactorily than any other the unusual frequency of abnormal presentations among malformed fetuses.

It is also felt that this study affords additional evidence to confirm the importance of deflexion attitudes in the etiology of abnormal presentations among normal fetuses.

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### Addendum

Since the present study was submitted to the editor, a paper on a related subject has appeared by Pendleton Tompkins (AM. J. OBST. & GYNEC. 51: 595, 1946). Dr. Tompkins uses a different approach, but arrives at similar conclusions concerning the causes of breech presentations.



In conformance with the recommendations of the Committee on Food and Nutrition of the National Research Council,<sup>3</sup> the superiority of the natural vitamins found in foods over factory products is emphasized, as is also the nutritional value of animal proteins. In order that iron metabolism may be adequate, meat (beef or lamb) or fish should be eaten once every day, and liver once or twice a week. One or two eggs should be included in the daily intake as well as two servings of cooked, green vegetables. The patient must be impressed with the fact that vegetables green in color contain, besides vitamins, more readily assimilable proteins and minerals. According to Stare and Davidson<sup>4</sup> the actual protein requirements during pregnancy cannot be definitely stated, but 10 to 20 grams of additional protein per day have been suggested as increased requirements.

The patient is warned not to eat an excessive amount of fruit. She should have the equivalent of one orange or half a large grapefruit or a serving of tomato juice for breakfast, and one serving later in the day of a cooked fruit, such as a sauce or a canned fruit salad without the heavy syrup. The foods mentioned are the sheet anchor of the diet, and to these the patient is permitted to add starches, sweets, and fats in limited amounts to balance the meals.

A gain of more than a pound in two weeks calls for reduction, not in the proteins and cooked vegetables, but in the quantity of such foods as ice cream, candy, pastries, cereals, macaroni, cheese, corn, potatoes, and bread. If the scale indicates an excessive gain, the patient is instructed not to eat between meals and to drink nothing but water between and with her meals. Tea and coffee may be taken in limited amounts. When the weight is not excessive, skimmed milk is permitted with meals. (Skimmed milk contains more calcium than whole milk.) The patient must adopt a philosophy of not eating all she wants at any meal, but leave the table hungry until her weight is under control. She is urged to weigh herself frequently, and to remember that the scale, and not her appetite, determines how much she may eat.

Any food that will relieve hunger has caloric value. It is impossible to ascertain the quantity of a proper diet in advance because there are three main factors which determine the results from the intake: digestion, assimilation, and utilization. It is well known that any one of these factors may vary from time to time even in the same individual and thus upset the calculations. Consequently, no set quantity of food or number of calories will give the desired results in all patients. Therefore, much of the time during office visits is devoted to a discussion of the diet in an effort to impress the patient with the necessity of being weight-conscious.

At each monthly visit the weight and blood pressure are obtained. The blood pressure is checked only once a month during the first seven months and twice a month the last two months, unless there is some indication for more frequent examination. The dietary advice is continued and the blood rechecked as often as necessary to determine whether any form of iron is needed or injections of liver extract should be administered. It is important that the blood be watched closely and the diet discussed frequently, otherwise the patient may

must convince the patient that safety and welfare of both mother and baby depend largely upon her cooperation. Minot<sup>2</sup> writes, "The partaking of proper food is excellent preventive medicine and upon it depends the integrity of man." Much will power is needed to follow a reducing diet with an intake that sometimes does not satisfy hunger. Many people, including some doctors, still harbor the erroneous notion that a pregnant woman must eat for two. Most patients believe that cravings for food during pregnancy must be satisfied or the baby will be deprived of nourishment. Likewise, there are too many physicians and dentists, not to mention patients, who cling to the old adage, "For every child a tooth," because they believe that the unborn baby can draw calcium from the mother's teeth. As a consequence of this fallacious reasoning many excess calories in the form of milk and fruit juices are poured into the expectant mother in order to resist demineralization of her teeth. One patient with toxemia of pregnancy referred to me at term showed a gain of 110 pounds during her pregnancy; that is, she went from a weight of 117 pounds at the time of conception to 227 pounds at term. Her teeth, poor to begin with, had been badly neglected because she believed that any dental work during pregnancy was likely to cause a miscarriage. When the patient's diet was investigated, it was found that her excessive weight was largely the result of a daily intake, during the last four months of pregnancy, of three quarts of milk and the juice of six oranges, prescribed in the hope of preventing further damage to her teeth.

It is necessary to explain to the patient that it is impossible for the baby to take any calcium from the mother's teeth, that the calcium in an adult's teeth is fixed, and that no form of diet can add to or take away calcium from the mother's teeth by way of the circulation. The patient, however, must see a competent dentist and have her teeth cleaned and cavities filled.

The patients here reported were given enough calcium daily (preferably in the form of a bone phosphate) to equal the calcium in a quart and a half of milk, with sufficient vitamin D to assimilate and utilize the calcium. Pregnancy and parturition in a healthy woman should be a normal process and should terminate with the mother unharmed and a live, healthy baby.

The prenatal care in this program is not markedly different from the general trend, except for a controlled diet and frequent observation of the condition of the patient's blood. Good prenatal care consists of good general hygiene, which includes a proper food intake, regularity of elimination, ample rest, and suitable exercise. It is understood that morbid processes found in a patient must be relieved as far as is possible. This calls for the various tests of organic function, and the discovery and removal of those factors which are recognized as predisposing to toxemia.

In my practice, on her first visit the patient is given a booklet on prenatal care which she is instructed to follow diligently. In this are listed the calorie values of 300 servings of food, vitamin tables, and an outline of daily diets for a week. Some little time is spent with each patient in an attempt to explain the purpose and importance of a well-balanced diet. She is told that the baby obtains its growth principally from proteins, minerals, and vitamins.

more a month) before the end of the seventh month of pregnancy showed sudden increases in the last two months of pregnancy notwithstanding a low caloric intake during that time. This sudden increase was the result of excessive fluid retention in the tissues. These patients revealed excessive weight loss by the tenth day post partum, and the weight six weeks post partum was about the same as the weight at the time of conception. This observation conforms quite closely to that made by Waters.<sup>13</sup>

Success in weight control seems to depend on the first seven months. If the patient lets her appetite get out of bounds during that time, toxemia is sure to follow in a certain proportion of cases. In all of the reports of pregnancies I have examined, toxemia occurred in about 4 per cent of the patients who gained 18 pounds or more.

The 1,000 women who followed the weight control program throughout their pregnancies were delivered without a death or a single instance of toxemia, pre-eclampsia, or eclampsia. In no patient did the blood pressure exceed 145 systolic or 85 diastolic. Edema was a negligible factor throughout the series. Only in rare instances was it necessary to advise a salt-poor diet because of edema of the ankles. In each of the few cases in which the salt-poor diet was prescribed and the protein intake increased, the edema disappeared in four to ten days.

The diet regime followed by these 1,000 patients naturally resulted in a higher protein intake. The gratifying results obtained by patients whose protein intake was higher than usual is in agreement with the conclusions of Leverton and McMillan,<sup>14</sup> who state, "Women whose intake of protein was augmented by receiving a 5-ounce serving of meat daily in addition to their self-chosen diets during the period from four months before delivery until three months after delivery had higher hemoglobin and red cell values, less edema, and better success in lactation than women who received no supplement."

In slightly more than a third of the patients there was a trace of albumin in an uncatheterized urine specimen sometime during pregnancy. Quantitative tests showed no more than 0.3 Gm. of albumin per 1,000 c.c. in twenty-four hours in any one specimen.

Serum globulin and serum albumin tests were made at random on a few of these patients. All tests were within normal limits. The serum globulin average was 2.7 mg. per cent. The serum albumin average was 4.17 mg. per cent.

There were no cases of puerperal infection, but there were two patients who had mild phlebitis. In each instance the temperature was normal before the tenth day postpartum and tenderness over the affected veins had disappeared. One of these patients had some swelling of her leg which did not entirely disappear for several months.

The progress made against toxemia of pregnancy in this series of patients who followed the prescribed diet is comparable with what has been accomplished in the prevention of puerperal infection since the advent of the sulfonamides.

During the same period of time that this series of 1,000 patients were cared for, 366 patients were under my care and are not included in the report. They may be divided into three groups:

drift toward seasonal foods such as corn and other starchy foods and may not eat an adequate amount of protein. This may result in anemia with its possible complications.

Thyroid extract is given to all patients who can tolerate it and whose basal metabolic rates indicate its need. If the patient's pulse is below 70, small daily doses of desiccated thyroid are ordered, even if the basal metabolic rate is within normal limits. The amount of thyroid is increased every fifth day until there is an indication of excessive dosage, when it is discontinued at once for four days. On the fifth day the thyroid intake is begun again with the dose equal to the last daily dose that did not disturb the patient. A therapeutic test of thyroid tolerance is thus obtained, and adequate dosage provided. In my opinion, this is the most reliable test for deficiency and administration of thyroid.

Occasionally a patient has considerable trouble in controlling her desire to eat. Benzedrine sulfate in doses of 5 mg. three times a day has often proved helpful. She is allowed to take even larger doses if it does not make her nervous or wakeful. She is told, however, that neither the thyroid nor the benzedrine will reduce her weight unless her caloric intake is reduced. The benzedrine will aid in allaying the hunger of most patients without untoward effect.

If this type of diet is followed, anemia is usually avoided. According to Dieckmann,<sup>5</sup> anemia predisposes to edema and toxemia. He also states:<sup>6</sup> "The albumin and globulin molecules are so large that they do not pass through the capillary walls. Because of this lack of permeability, albumin and, to a lesser extent, globulin, exert colloid osmotic or oncotic pressure within the capillary." If this is true, and with our present knowledge there is little reason to doubt it, a high protein diet should tend to prevent edema. Strauss<sup>7</sup> writes: "If the expectant mother does not eat enough protein food, meat, eggs, fish, and milk, instead of losing weight she gains excessively, but this weight consists of water or occult dropsy." He continues with the statement that this may lead to eclampsia, but in a more recent article he declares that a reduction of the sodium intake may be necessary to cause the edema to subside. The same author also observes that there is a hypoproteinemia in toxemia of pregnancy.<sup>8</sup> According to Arnell<sup>9</sup> "Protein inadequacies . . . were aggravated during pregnancy by restriction of meat, eggs, and milk either self-adopted or carried out on medical advice." Williams<sup>10</sup> states that the incidence of toxemia in pregnancy was twice as great in one group of pregnant women whose protein intake was 60 to 70 Gm. daily as compared with a similar group whose protein intake ranged from 110 to 120 Gm. daily. McCance, Widdowson, and Lehman<sup>11</sup> write: "In the presence of high protein intake, 15 per cent of the calcium was absorbed as compared with an absorption of only 5 per cent of the calcium in the low protein diet." Rossenbeck<sup>12</sup> found a slight increase in the sodium content of the muscle in normal pregnancy and an enormous increase in eclampsia.

If the gain of an organically sound patient who had a normal weight at the time of conception is not allowed to exceed two pounds any one month up to the eighth month, she will not have retention of fluid in her tissues and, consequently, she will not acquire a sudden gain of weight in her last two months of pregnancy, unless there is excessive caloric intake. On the other hand, many of those patients observed who gained excessive weight (up to four pounds or

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1. Those not organically sound because of hypertension or diabetes.
2. Those overweight at the beginning of pregnancy.
3. Those who could not or would not cooperate.

Essential hypertension	15	Fetal Mortality
Hypertension (nephritis)	2	1 ( 6.0%)
Overweight before conception	89	
Initial blood pressure over 145/85	87	9 (10.3%)
Overweight	66	
Excessive gain	39	
Overweight before conception	22	3 (14.3%)
plus excessive gain		
Failed to cooperate	253	

Among the first 800 of the 1,366 cases, there were 200, or almost 25 per cent, who failed to cooperate. Of the next 400 there were 10 per cent who did not cooperate, and in the last 166 cases 2 per cent failed to cooperate. Better success in the control of the patients' weights among the last 166 patients was probably due to better advice as a result of progress in experience of the author.

Birth weights differed from the usual statistics in only one respect: the average weight at birth was slightly less than 7 pounds. There were no large babies. One baby whose parents were both over six feet tall weighed 9 pounds, 2 ounces.

TABLE I. FETAL MORTALITY IN CONTROLLED GROUP AS COMPARED TO THAT IN THE GROUP NOT CONTROLLED, OVERWEIGHT, OR NOT ORGANICALLY SOUND AT CONCEPTION

	GROSS MORTALITY* (PER CENT)	CORRECTED MORTALITY† (PER CENT)	CORRECTED MORTALITY‡ ADJUSTED TO PRE- MATURITY (PER CENT)
1000 cases	2.4	1.6	0.6
366 cases	7.9	4.9	3.5

\*Pregnancy of 5 months or over.

†Pregnancy of 28 weeks or more.

‡Exclusion of infants 32 weeks or less in utero.

### Summary

1. This report is based on records of 1,366 obstetric patients, of whom 1,000 when first seen were within normal weight range and organically sound. They revealed an initial blood pressure within normal limits and cooperated in a controlled diet regime.

2. Successful management depends on two factors: (1) the patient must understand the purpose of the program; (2) the patient must cooperate.

3. One thousand patients whose weight was controlled by a restricted diet developed no toxemia, no pre-eclampsia or eclampsia. There were no maternal deaths.

4. Patients following a prescribed diet, high in protein, have less anemia, less edema, and less tendency to develop toxemia or eclampsia.

5. The fetal mortality rate in this series was one-sixth the fetal mortality of the uncontrolled group.

6. There were no large babies.

TABLE I. PATHOLOGIC DIAGNOSIS

Solid Carcinoma	5
Papillary cystadenocarcinoma	62
Pseudomucinous cystadenocarcinoma	7
Granulosa cell tumor	6
Hodgkin's sarcoma	1
Primary luteoma	1
Embryonal sarcoma	2
Malignant teratoma	1
Fibro-sarcoma	1
Sarcoma	2
Krukenberg tumor	1
Adenocarcinoma, secondary to fundus uteri	4
Adenocarcinoma, secondary to colon	4
Unclassified	3

cancer of the ovary is rare if sarcomas are excluded. As the growth usually spreads by implantation and contiguity, distant metastases were found in a small percentage only in this series. Forty-four had ascites at the time of operation, while 49 did not.

*Age Incidence.*—Sixty-three per cent of our patients were between the ages of 40 and 60 years. The youngest was 19, while the oldest was 75 years of age. The average age was 47 years; two were under 20 years of age; one of the two had a colloid carcinoma which was unilateral, and from which she died in six months; the other had a unilateral cystadenocarcinoma, and is still alive two and one-half years after simple unilateral salpingo-oophorectomy. Most patients between 70 and 75 years of age died in less than six months following operation. However, there is one patient, aged 71 years, who had a simple removal of a unilateral papillary cystadenocarcinoma, and is still alive three and three-fourths years after operation.

*Menstrual History.*—Most of the patients had normal onset of menstrual life. Forty-four per cent were still menstruating, while 56 per cent had already passed through a normal menopause. Twenty-nine per cent had some disturbance of the menstrual cycle, mainly metrorrhagia.

*Marriage and Pregnancy.*—Of this series 24 were single, and 76 were married. Forty-one per cent were nulliparous, 19 per cent had one child, while one patient had 11 offspring. Fourteen women had a total of 23 miscarriages. This series showed a high incidence of sterility. Only three-fourths of the married women had borne children, and 18 per cent had aborted.

*Signs and Symptoms.*—The insidious onset and progress of the tumor are shown by the fact that 68 per cent of all patients were considered incurable when first seen. Over 18 per cent had symptoms less than one month before presenting themselves for examination. Thirty-one per cent of all cases were examined within two months of the appearance of the first symptom.

Seventy-five per cent of the series had abdominal pain; 44 per cent had abdominal enlargement; 32 per cent had loss of weight; 29 per cent had some form of abnormal vaginal bleeding; 18 per cent had marked constipation; 17 per cent had a palpable tumor; 17 per cent had vomiting; 11 per cent had dyspnea; 9 per cent had frequency of urination; 4 per cent had diarrhea. There were diffuse abdominal pains, and pains localized to the epigastrium, lower quadrants, and lower back. Usually the pain was vague and intermittent when first noticed, but rapidly became more severe and constant. Several patients came into the hospital with such severe pain that they were diagnosed as acute appendicitis, or other acute abdominal crises. Abdominal enlargement caused least concern to the patient, many believing it was due to fat. The presence of

## A REVIEW OF ONE HUNDRED CASES OF OVARIAN CANCER

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WHILE considerable progress has been made in the diagnosis and treatment of cervical and fundal malignancies, the same cannot be said of ovarian malignancies. With an incidence of 10 per cent of all ovarian neoplasms, and with a mortality rate that has been, and remains, appallingly high, ovarian cancer constitutes a major gynecologic problem. Early diagnosis is particularly difficult since a large percentage of patients is incurable before symptoms manifest themselves. There have been too few series reported in sufficient detail from which to draw reliable conclusions. Can we estimate the survival time from the histologic grading of the malignant growth? Can clinical grouping be used as an index for the prognosis of ovarian cancer? What effect has radiation on survival time? In an attempt to answer this riddle, the writer has presented a clinical review of 100 cases. Thirty-five cases could not be traced. The other 65 were traced from treatment to death, or to a survival as long as ten and two-thirds years.

The material for this review was obtained from records of proved cases of ovarian cancer treated at the Elizabeth Steel Magee Hospital and the St. Francis Hospital in Pittsburgh, Pennsylvania, over a period of fifteen years (1929 to 1943). Where possible, all diagnoses were confirmed by microscopic section.

In this series, 52 tumors were determined to be bilateral, while 32 were unilateral. One adenocarcinoma occurred in an ovary which was also the seat of a dermoid cyst. A Krukenberg tumor appeared to be primary in the ovary as no other lesion could be discovered at the time of operation. There were eight secondary growths in the ovary, four being secondary to the fundus uteri, and four secondary to the colon. The types of tumors and their numbers are shown in Table I.

In addition to the ovarian malignancy there were 11 fibroid uteri, one fibroma of the opposite ovary, 12 pelvic infections, one acute appendicitis, 10 ovarian cysts, two of which had twisted pedicles, two chocolate cysts, three pelvic endometriomas, and one retained doughnut pessary.

The gross appearance of ovarian cancer is often bewildering. An attempt to classify such malignancies as solid or cystic forms is unsatisfactory, for many that appear cystic have solid cores, while the solid-appearing tumor is often riddled with cysts. Thus, we see all kinds, large, small, papillary, smooth-walled, cystic, solid, solid and cystic, yellow, white, grey, blue, red, etc. In some cases transition from a malignant papillary cyst to a solid tumor seems to occur. In this series, the majority seemed to arise from papillary cystadenomas. Five multilocular pseudomucinous cysts contained solid malignant areas, and three of these had ruptured, giving rise to pseudomyxoma peritonei. Solid primary



II, the tumor is completely removable, but with some disturbance of other structure, such as adhesions to, or involvement of other tissues which can be removed. In clinical Group III, the tumor is only partly removable on account of extension to near-by structures which cannot be removed. This group includes all cases in which a partial operation is done with the hope of destroying or delaying the growth of the remaining part by irradiation. In clinical Group IV, the tumor is irremovable because of extensive involvement of adjacent parts or because of distant metastases. Only a biopsy specimen can be obtained at operation. Table II below shows the average survival time according to clinical groups.

Clinical Groups I and II have survival times much greater than Groups III and IV. There was an immediate mortality of seventeen. This includes all who died within two weeks of operation. Four of these belonged in Group IV, eleven belonged to Group III; one belonged in Group II; one belonged in Group I. The advanced cases were recognized as bad risks, but were subjected to operation in the hope of relieving a desperate situation.

The substantial early mortality rate explains why many patients did not receive radiation. As stated earlier, the survival time in patients receiving operation plus radiation was three times as great as cases receiving operation alone. Before we drew the obvious conclusion that radiation triples survival time, let us examine the composition of the two groups. Fifty-seven per cent of the 19 cases receiving operation and radiation were in Groups III and IV, while over 97 per cent of the 39 cases receiving operation alone belonged in Groups III and IV. However, the conclusion that radiation prolongs life substantially is borne out in this series. Of the 65 patients traced to date, 13, or 20 per cent, are still alive. Two of the survivors are in Group I, seven are in Group II, four are in Group III.

TABLE II

GROUP	NUMBER	NUMBER TRACED	AVERAGE SURVIVAL TIME
I	11	3	38 months
II	18	13	36 months
III	45	30	19½ months
IV	19	15	5½ months
Total	97	61	24 months

TABLE III. THE SURVIVAL RATE AFTER TREATMENT

TIMES SURVIVED	CLINICAL GROUP			
	I	II	III	IV
0 to 6 months	1	3	16	10
6 to 12 months	0	2	3	8
1 to 2 years	0	4	2	2
2 to 3 years	1	0	1	1
3 to 4 years	1	1	2	0
4 to 5 years	0	2	1	0
5 to 6 years	0	0	0	0
6 to 7 years	0	0	1	0
7 to 8 years	0	0	1	0
8 to 9 years	0	0	0	0
9 to 10 years	0	0	1	0
10 to 11 years	0	1	0	0

According to pathologic classification, six of the surviving patients had papillary cystadenocarcinomas; two had pseudomucinous cystadenocarcinomas; one had a solid adenocarcinoma; one had a malignant teratoma; one had a granulosa-cell tumor; and one had an embryonal sarcoma.

Of nine patients subjected to exploratory laparotomy and removal of biopsy specimen, there was an immediate mortality of three. One died following biopsy of an inguinal node. These advanced cases cannot be explored with impunity.

a palpable tumor was the sole sign in five cases. Cases presenting frozen pelvis and abdominal fluid were diagnosed correctly most frequently. Pelvic masses inseparable from the uterus and without abdominal fluid were often felt to be fibroids. A considerable number were diagnosed as simple ovarian cysts, with the malignant nature discovered after the abdomen was opened.

*Treatment and Results.*—Surgery was attempted in all but five cases which were considered utterly hopeless. Seventy-six cases received abdominal operations in which more or less of the primary and metastatic growth was removed. Nine had exploratory laparotomy with removal of one or more small pieces of tissue for examination. Two had paracentesis only; two had paracentesis and peritoneoscopy; four had exploratory laparotomy plus removal of biopsy material, and subsequent paracentesis; two had laparotomy for removal of pseudomucinous material. In 39 cases supravaginal or total hysterectomy was performed, usually with removal of both ovaries. Nineteen had unilateral or bilateral removal of adnexa only. None of the tumors was tapped deliberately, although several ruptured during an attempt to free them. The small intestine was resected in five cases, and colostomies were performed four times.

Postoperative radiation has been used freely, particularly in the past ten years. In 65 cases traced, 19 had operation plus radiation, 39 received operation alone, two had radiation alone. Five cases did not receive treatment of any kind. The average survival time after operation plus radiation was 35.3 months; after operation alone, 11.7 months; after radiation alone, 1.5 months; without treatment of any kind, 2.5 months. The group receiving operation alone contained the advanced cases, some of which did not survive long enough to receive radiation therapy. The group receiving x-ray alone was too far advanced to undergo operation, or refused operation. The group that did not receive any treatment included those cases that did not tolerate x-ray. Of these two latter groups all were dead within six months of arrival at the hospital.

Histologic grading proved of little importance in prognosis. All carcinomas primary in the ovary were placed in three grades. In Grade I there is good glandular formation with well-differentiated columnar epithelium. The mature type of structure is maintained throughout, except in areas where early malignant changes are going on, such as piling up of epithelium or invasion of the stroma. This is the least malignant type. In Grade II, glandular and papillary structures are still present, but they are poorly developed. The columnar epithelium is not so well differentiated. There are moderate variations in the size and shape of the cells, nuclear changes, and more extensive invasion. This is a moderate degree of malignancy. In Grade III there is little evidence of glandular and papillary structure, the fields showing practically solid carcinoma. This is the most malignant type.

One of our longest survivals is a Grade II malignancy, being well almost eleven years after operation. Another Grade III malignancy, in the same age group, survived only three and one-half months. A 24-year-old patient with a Grade I malignancy died in four months with a recurrence. Another Grade I malignancy, in a patient 22 years old, is well three and one-half years after operation. A study of a small group of patients, all in the same age group, gave the following inconclusive figures:

Grade I—six cases had an average survival time of thirty-seven and two-thirds months.

Grade II—eleven cases had an average survival time of twelve months.

Grade III—seven cases had an average survival time of twenty-six and one-third months.

Clinical grouping seemed to be of more importance in making a prognosis. In clinical Group I, the tumor is completely removable, and is without gross involvement of any other structure at the time of operation. In clinical Group

## SOME OBSERVATIONS UPON THE Rh FACTOR IN PREGNANCY\*

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SINCE the discovery of the Rh factor in human blood by Landsteiner and Wiener in 1940<sup>1</sup> and its relationship to erythroblastosis fetalis by Levine,<sup>2</sup> there have been many articles upon the subject in the literature, lay as well as medical. Since the occurrence of the latter is not too frequent, it has seemed worth while to summarize the results and mention some of the problems encountered during a period of fifteen months in the obstetrics department of a general hospital. Our laboratory has been doing the Rh determinations and kindred studies for us since September, 1944. From that time until December, 1945, there were six cases of erythroblastosis fetalis encountered in 1,682 deliveries, for an incidence of one case per 280 deliveries. These cases came from the delivery of 75 Rh-negative mothers, with an incidence of one in 12.5 Rh-negative women.

During this period there were 1,129 Rh determinations with 10.36 per cent of negatives. The apparent discrepancy between this number and the original 15 per cent incidence among whites reported by Landsteiner and Wiener<sup>3</sup> can be explained in two ways. First, there are a few Negro patients included, but more important than this is the fact that the original work classes Rh' and Rh'' as negatives while they are now screened out and classed where they belong among the Rh positives.

It would be extremely presumptuous to attempt to draw any conclusions on the basis of this small series of cases. However, certain seemingly obvious facts have come to our attention during the treatment of these cases, and also while managing some other cases of Rh-negative women in pregnancy. In view of the many divergent opinions to be found in the literature, it has seemed worth while to add our findings with the hope that, when grouped with several similar series from other institutions, we may all thereby sooner reach a rational basis for the management of and therapy in this comparatively infrequent, yet important condition.

In attacking the problem, it would seem that a beginning might best be made by reviewing the management of the Rh-negative woman who is pregnant. During this period of fifteen months the writer has delivered 12 Rh-negative women in his own practice, plus at least one (Case 5) for another. Omitting the latter, as her history was not known before delivery, there were two primigravidas, both with normal babies. This was to be expected, as damage to the baby in a first pregnancy is not only extremely unusual, but also portends a very grave, if not hopeless, outlook for future pregnancies, in the present state of our knowledge. The remaining ten cases were multigravidas and one (Case 2) delivered an erythroblastotic baby. One of these was not seen until she was

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### Discussion

It is seen that the greatest difficulty is encountered in anticipating results from either radiation or operation, as many factors are involved. Not only are there many different pathologic aspects to each case, but the extreme variability of the different parts makes each case a definite study in itself. The duration of symptoms, the surgical treatment rendered, the radiosensitivity of the tumor cells, the reaction of the patient herself, all must enter into consideration when prognosis is attempted.

One hundred cases of ovarian cancer were analyzed. Four of these patients were Negroes. Most of our patients were between 40 and 60 years of age, and more than half were past the menopause. There was a high incidence of sterility in this series, 41 per cent being nulliparous. The most commonly associated pathology was ovarian cyst, fibroid and pelvic infection. The duration of symptoms is so short that about two-thirds of all patients arrived at the hospital when hopelessly involved. One-third of this series had symptoms under two months. All but five patients had some type of operative procedure carried out by 18 different operators. In three-fourths of the cases only part of the tumor could be removed; while in one-fourth, all of the tumor seen at time of operation could be removed. There was immediate mortality of one-sixth of all cases treated. Three deaths had causes unrelated to malignancy. The survival time was three times as great when all the tumor could be removed.

### Conclusion

1. Histologic grading is of little value in prognosis.
2. Symptoms occur so late that early diagnosis is almost impossible.
3. The majority of patients are hopelessly involved when first seen.
4. The degree of removability of the growth plus use of radiation largely determines the survival time.
5. Postoperative radiation often increases the comfort, and improves the psychologic state of the patient.
6. The curative value of radiation is discouragingly low.

Despite the very discouraging end results in advanced cases of malignant disease of the ovary, it is our impression that removal of the primary growth enables the patient to carry on a life of usefulness in comfort, sometimes for years. This makes the operation worth while. We will report cases illustrating this point, and discuss this phase of the question in a subsequent paper.

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glutination on the sixth day when, as if from heaven, the first B negative blood of a man reached the laboratory. We injected 75 c.c. of his blood into the peritoneal cavity, rather than lose it when the intravenous cannula became clogged. Whether from exhaustion of crying or from the mode of administration, the baby developed a shocklike reaction after this, and was put into an oxygen tent overnight. There was no fever or hemoglobinuria, and the red blood count rose to 4,200,000 on the ninth day, again falling to 2,480,000 by the twenty-first day. On this date one of our original B positive donors was found compatible, and 75 c.c. of his blood were given by vein without reaction, sending the count above 5 million for two days, with a drop to 4,200,000 at discharge on the thirty-second day. This baby never went to breast and was put on a biolac formula from the start. Beginning the twelfth day she received 20 drops, later 30 drops, twice a day of feosol elixir and 25 mg. daily of ascorbic acid. She survived an attack of pertussis beginning two weeks after her discharge, and has developed normally to date.

CASE 3.—Mrs. E. H. had a miscarriage thirteen years previously, at which time she was transfused, with her husband as donor. She went into labor a few days past term, and the fetal heart was heard at the beginning. After a fourteen-hour labor she delivered a macerated female infant. Her blood gave a strong blocking reaction before and still blocked at a dilution of 1:40 five months later.

CASE 4.—Mrs. McC. had had a boy living and well, and the second was a girl who died on the third day. She has two Rh-negative sisters who have each lost several babies elsewhere. This baby, a full-term female, had on the first day a red blood count of 2,480,000, and 77 normoblasts per 100 white blood cells. She was given 40 c.c. of Rh-negative group O blood on the third and fifth days intramuscularly. The blood showed a red blood count of 2,410,000 on the seventh day, with 44 normoblasts and 3 megaloblasts. On the ninth day she got 100 c.c. of Rh-negative O blood by vein, and the count rose to red blood cells, 2,800,000, with 23 normoblasts on the eleventh day and 3,130,000 on the fourteenth day. By the twenty-fourth day there was a drop to a red blood count of 2,670,000, followed by a slow rise to 3,650,000 when discharged on the fortieth day. Reports since indicate that this baby is normal. The breast milk gave a 4 plus agglutination at 1:1 dilution one week post partum, while on the fourteenth day the maternal blood gave a 4 plus at 1:40, and at four weeks was the same reaction at 1:80 dilution.

CASE 5.—Mrs. McK. was transfused with her father's blood following a 3-month miscarriage a year previous to this delivery of a full-term female which had a slight yellowish tinge at birth. As she was delivered by the writer for another doctor who was ill, this history was not uncovered nor was anything done until the baby became intensely jaundiced on the second day. On this day we found a red blood count of 2,340,000, normoblasts 52 and megaloblasts 4 per hundred white blood cells, and so 60 c.c. of citrated Rh-negative O blood containing 3 c.c. of Whitebsky's A and B substances were given by vein. On the third day there was a red blood count of 3,680,000, and 3,730,000 on the fourth day. There were no normoblasts found on the fifth day, but a gradual drop to a red blood count of 2,400,000 on the fourteenth day when we again transfused with 50 c.c. of Rh-negative O blood citrated, and containing 3 c.c. of A and B substances. The count gradually rose to 3,230,000 when discharged on the twenty-first day, and the baby has been reported normal since. The patient's father (her donor) as well as her husband and the baby are all Rh positive. Her milk had agglutinins when undiluted, while her blood blocked

admitted to the hospital in labor, but all of the others were checked one or more times for the presence of anti-Rh agglutinins and/or blocking antibodies.<sup>4, 5</sup> No particular concern was felt for the baby in the six cases where the maternal serum was negative for both, and our judgment was justified by the delivery of a normal baby in each case. In three cases, however, the maternal serum was found to contain agglutinins, and so preparations were made for possible transfusion of the baby at birth. There were no cases in this group who showed blocking antibodies, and the agglutinins were demonstrable only in the undiluted serum of two cases. In these cases, a red count and smear of the cord blood assured us that we need have no further anxiety concerning these babies. The one case with a rather high titer of agglutinins will be presented later (Case 2). Earlier reports stressed that about half the cases of erythroblastosis occurred where few, if any, agglutinins could be demonstrated in the maternal serum. This inability to foretell the outcome has been almost, if not completely, removed by Wiener's<sup>5</sup> discovery of blocking antibodies. Since our work began subsequent to this publication of his, all of our Rh-negative maternal sera were checked for blocking antibodies at the same time that an agglutinin titer was run, and it might be noted at this point, that in all six cases of erythroblastosis fetalis the mother's blood showed either one or both.

### Case Reports

CASE 1.—Mrs. H. had two normal living Rh-positive children and has had two miscarriages. This baby, a male, was delivered at term and became jaundiced on the second day. Blood studies were red blood cells 3,700,000, hemoglobin 75 per cent, white blood cells 26,500, and 53 normoblasts per 100 white blood cells. The jaundice deepened and the anemia increased, and on the fifth day the baby was given 50 c.c. of Rh-positive blood by vein. Following this there was a severe reaction, the temperature rose to 104° F., hemoglobinuria developed, and the jaundice deepened to an actual green color. On the ninth and twelfth days, respectively, he was given 50 and 100 c.c. of Rh-negative blood, and on the latter day he was also removed from the breast when the mother's milk gave a 4 plus agglutination at a 1:5 dilution. The baby improved from this time on and was discharged on the twenty-fifth day, above birth weight, but with a red blood count of only 3,500,000. There is nothing further known of this baby.

CASE 2.—Mrs. S. had an early miscarriage, then a premature boy who survived and is Rh positive, and a girl who died on the second day with postmortem findings typical of erythroblastosis fetalis. The patient was referred to the writer when in the second month of pregnancy, and at that time no agglutinins were demonstrable. They were present by the fifth month and gave a 4 plus agglutination at a dilution of 1:160 by term when this baby, another girl, was born. We could see no jaundice at first, but within a half hour it was readily apparent. The cord blood showed her red blood count to be 3,530,000, normoblasts 36 per 100 white blood cells, and an icterus index of 150, and was Rh positive, group B. She was given 100 c.c. of citrated O negative blood to which had been added 3 c.c. of Witebsky's A and B substance<sup>6</sup> by way of the umbilical vein. Despite increasing jaundice, the red count rose to 3,800,000 on the third day. The count then began to fall, reaching 2,330,000 on the sixth day, even though the baby was given 50 c.c. of group O positive blood subcutaneously on the fifth day. Two group B positive donors had been rejected because of ag-

3. All Rh-negative multigravidas and those who have been transfused either with Rh-positive or unknown blood should be tested for agglutinins and blocking antibodies at least once during the last three months of pregnancy. Wiener's conglutination test,<sup>7</sup> covering both of these as it does, would seem sufficient.

4. In those cases with either marked agglutination or blocking reaction, preparations should be made for a full blood study of the infant in the delivery room, and, where indicated by red count of 2,500,000 or less, Rh-negative blood should be given via the umbilical vein before tying the cord.

5. Whenever transfusion is indicated, Rh-negative blood should be used. While we have contemplated using a suspension of washed maternal cells, we have not yet been forced to do so. In the writer's cases, whenever group O blood was used Witebsky's A and B substance was added.

6. As to the route of administration—once the cord is tied we have found a 22-gauge cannula in a surface vein with pressure behind the blood supplied by the syringe of an intravenous anesthesia outfit to be the best. The metal valve should be new, as contact with the material used in anesthesia may leave a sulfur deposit and thus cause some difficulty.

Final results almost equal to intravenous administration were obtained by one intraperitoneal injection. This was done as a last resort to avoid the loss of an irreplaceable blood donation when the intravenous cannula and vein became obstructed while trying to use a gravity flow. The baby was worn out from this trial and, whether from fatigue or from the method of administration, went into a mild state of shock after returning to the nursery. While the method is simple from the standpoint of technique, we have hesitated to repeat it because of our uncertainty concerning the cause of the shock.

Intramuscular and subcutaneous administration was used a few times with questionable results.

7. Babies with erythroblastosis must not be allowed to nurse, as the breast milk contains anti-Rh agglutinins. Adequate nutrition probably requires a high iron intake with vitamins in addition to a modified milk formula.

8. Prognosis for these affected babies must remain guarded in view of neurologic residua such as spasticity and mental retardation attributed to kernicterus and reported by, among others, Leonard<sup>11</sup> and Docter.<sup>12</sup> The few babies so far observed by us seem to be developing normally, although they are all still under one year of age, and these residua are sometimes not observed until as late as two years of age.

9. Outlook for future babies seems to depend, at the present time, upon two factors. First, another baby might be Rh negative with no danger of trouble, and second, even if the baby is Rh positive, it may survive with treatment. This latter outcome would seem to be favored by deferring the pregnancy at least until the maternal blood is free of agglutinins and blocking antibodies.

10. In view of the slender margin of safety encountered with these full-term babies, we are opposed to the induction of labor before term with the added dangers of prematurity to be overcome.



through a 1:20 dilution and gave a positive 'conglutination' test, but there were no demonstrable agglutinins, all on the second day post partum.

CASE 6.—Mrs. W. has three Rh-negative children living, her fourth is Rh positive. She was aborted in the third month of her fifth pregnancy and in this, her sixth, she delivered a boy at term which developed jaundice and petechial hemorrhages and died in four and one-half hours. His spleen and liver were enlarged, but death occurred before any treatment was instituted. The maternal blood on the following day showed a positive conglutination and complete blocking through a dilution of 1:20, but no demonstrable agglutinins.

Mention has already been made of pregnancy in Rh-negative mothers, but because of its similarity to at least one of those above, the following case is given in detail.

CASE 7.—Mrs. V. was referred to the writer from out of town because of her history which was: one girl living, three spontaneous early abortions, following the second of which she received a blood transfusion. Her fifth pregnancy yielded a premature girl who died on the second day. The baby vomited green fluid but had no jaundice or edema; and when the mother's blood was sent to this city and reported to be Rh negative, she was told that this was the cause, and was given a very poor outlook for further pregnancies. Her blood at the first visit ten weeks before delivery, and again three weeks before delivery, showed no agglutinins by either tube or slide<sup>8</sup> technique, nor was there any demonstrable blocking reaction. On the basis of these blood findings, we assured the patient in advance that her baby would probably be normal, and this assurance was borne out by the delivery of a normal Rh-positive boy at term. An interesting sidelight—blood from the donor for the transfusion proved to be Rh negative.

### Discussion

From the above small series of cases some impressions have been gathered. If they are further strengthened by the experiences of others, as well as by our own further observation, they may become rules of treatment. However, it is again emphasized that they are still only impressions. Certain rules of conduct would likewise seem indicated by our experience and will also be included, for what they may be worth, in chronological order of caring for a case of pregnancy.

1. All pregnant women should have an Rh determination at the same time that their blood test for syphilis is done. Here we agree with Halperin, et al,<sup>9</sup> for, in 1,682 deliveries, we have apparently salvaged four babies that would otherwise have probably been lost. Because of these results we have the temerity to take exception to Wiener,<sup>10</sup> who would limit the Rh determinations because of a shortage of testing sera. It might well be noted here that we have been able to get good testing serum from several of these mothers and in quantities sufficient not only for our own needs, but also to supply others.

2. A careful history of previous transfusions as well as pregnancies should be taken on all pregnant women found to be Rh negative, and, when possible, the donor's blood should be tested for the Rh factor before delivery. A plea might well be inserted here that only Rh-negative blood be transfused into any Rh-negative woman who has not yet reached the end of her reproductive life.



## HEMOLYTIC DISEASE ASSOCIATED WITH THE Rh FACTOR IN TWIN PREGNANCIES\*

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ON MARCH 23, 1945, we delivered a primipara of twins, the first a normal healthy male, the second a stillborn macerated female presenting a typical picture of hydrops fetalis. Rh studies on the blood of the parents and the surviving child confirmed the diagnosis and led us to a perusal of our records of stillbirths and neonatal deaths in multiple pregnancies to study similar instances of erythroblastosis occurring in twin pregnancies. One hundred ten multiple pregnancies (one hundred nine twin, one triplet) were reviewed. In 22 cases, one or both children were stillborn or neonatal deaths. Sixteen were eliminated from further investigation because of incompleteness of records, grand multiparity mitigating against Rh incompatibility as a factor, absence of clinical signs of hemolytic disease of the newborn, or the presence of some definite causation unrelated to the Rh factor. The remaining six were studied clinically and serologically in so far as the limitations of our antisera would permit, and the results are herein presented.

Stratton, Langley, and Lister<sup>1</sup> have reported an Rh-negative mother who in her second pregnancy bore twins who were Rh positive but of different genotypes. The female child was normal. The male died on the fourth day of hemolytic disease.

Aaburg and Roby<sup>2</sup> describe the case of a woman who in her third pregnancy produced a male and female twin which presented two varieties of erythroblastosis (the first icterus gravis, the second hydrops). Both were Rh positive, the mother Rh negative. This case strengthens an impression which we derived from a study of one of our cases (No. 3) that there is a difference in the severity of effect in twins exposed to Rh antibodies, although in our own the offspring were monozygotic and in the one recounted by Aaburg were dizygotic.

Wiener<sup>3</sup> reports a twin pregnancy (the patient's eighth) in which the male twin was Rh negative and normal and the female died within thirteen hours of icterus gravis.

The incidence of fetal hemolytic disease resulting from the deleterious effect of transmitted maternal antibodies is difficult to determine. The combination of an Rh-negative wife and an Rh-positive husband occurs once in about thirteen marriages of white people.<sup>4</sup> Not every Rh-negative person exposed to Rh-positive blood becomes sensitized to the Rh factor. Individuals differ in the ease with which they can be sensitized, probably depending on some hereditary constitutional quality, so that in the average only about one in 25 to 50 Rh-negative persons exposed to the Rh antigen becomes sensitized. Occasional occurrence of hemolytic disease when the mother is Rh positive has been attributed to subtypes of Rh and the Hr factor.<sup>5</sup> The mere fact that the patient's blood is Rh negative is not proof that Rh incompatibility is responsible for the pathologic state. One must prove in addition that sensitization to the Rh factor has occurred. To do this, facilities for determining the presence of blocking as well as agglutinating antibodies are necessary.<sup>5</sup> Blocking antibodies are prob-

\*Read before the Pittsburgh Obstetrical and Gynecological Society, Feb. 4, 1946.

### Summary

No final conclusions are presented. We have listed some impressions formed as a result of treating six cases of erythroblastosis fetalis with the hope that, when combined with the experience of others, they may serve as a basis for the future management of Rh-negative mothers and their babies.

The writer wishes to express his thanks and appreciation to Drs. A. C. Williamson, Joseph Loughrey, and J. R. Johnston for permission to present their cases, and to Mrs. Bettina B. Carter for her invaluable assistance with the many blood determinations.

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In Case 2 the pregnancy was full term and uncomplicated. The first child was delivered by outlet forceps. He was quite anemic but survived with massive doses of vitamin K. The second was a macerated fetus with an edematous bloated body and a shapeless cranium. Follow-up three and one-half years later revealed the survivor to be physically fairly well developed, but of a mental age of about six months. Wiener<sup>5</sup> has referred to the occurrence of feeble-mindedness as a result of erythroblastosis and ascribes it to the occurrence of kernicterus or portal cirrhosis. This case also occurred in a first pregnancy without previous sensitization. It can be logically assumed that presence of monozygotic Rh-positive twins will result in a proportionately increased response within the maternal circulation.

### CASE 3.—

Father Rh positive		Mother Rh negative		First Twins Rh-positive male Rh-positive female		Second Twins Rh-positive female Rh-positive female stillborn
*Rhrh	+	rhrh	=	50% rhrh	+	50% Rhrh
			or			
RhRh	+	rhrh	=	100% Rhrh		

The first twins of this mating in Case 3 are a normal boy and girl past six years of age. The second set was born three and a half years ago. They were monozygotic twins born some weeks prematurely. The first girl weighed 4 lb., 13 oz., and exhibited a moderate anemia at birth. She survived after prolonged hospital care and is now apparently normal. The second child was stillborn, smaller, and presented the typical picture of an ieterus gravis. The accepted criteria of erythroblastosis are present in this family, the manifestations becoming evident after sensitization by the first set of Rh-positive twins. The second twins again demonstrate varying response to antibody exposure or perhaps a difference in priority or accessibility to the maternal antigens.

### CASE 4.—

Father Rh positive		Mother Rh positive		First Child Rh-positive female		Twins Rh-positive female Rh-positive female stillborn
*Rhrh	+	Rhrh	=	25% RhRh + 50% Rhrh	+	25% rhrh
			or			
RhRh	+	Rhrh	=	50% RhRh + 50% Rhrh		
			or			
RhRh	+	RhRh	=	100% RhRh		

In Case 4 this patient had had a spontaneous abortion between her first and second pregnancies. The first child was quite normal. The twins were born at thirty-four weeks. The stillborn female was small, compressed, with parchment-like yellow skin, a picture of fetus papyraceous. The survivor weighed 3 lb., 14 oz., and was not vigorous. The head was disproportionally large with wide fontanels. A difficult feeding problem was presented and hospitalization was prolonged. At eighteen months the child is physically well developed but mentally greatly retarded. This case is included because of its similarity to Case 2. The history is fairly typical of Rh incompatibility which is, however, disproved by the serologic findings. The unhappy result in the living twin must be conceded to simple prematurity unless we admit the possible responsibility of a blood factor which we were unable to determine.

\*Refers to Mendelian group in Table I.

ably more significant of hemolytic disease because they are smaller and hence traverse the placental barrier more easily.<sup>3</sup>

Ideally, one would have access to antisera which would react with the 21 genotypes of the Rh factor which are theoretically possible.<sup>10</sup> Practically, this is not feasible. As a matter of fact, we have had to discard specimens of the common human anti-Rh sera because they were not sufficiently potent to give reliable reactions. We agree with Levine that a pooling of material for the production of antisera in every community would be advantageous in maintaining adequate supplies of the various types.<sup>6</sup> Our serum is the standard anti-Rh, now designated anti-Rh<sub>1</sub> containing the agglutinins anti-Rh and anti-Rh<sub>1</sub>.

TABLE I. MENDELIAN INHERITANCE OF DOMINANT CHARACTERISTICS

1.	rhrh	rhrh	=	100% rhrh			
2.	Rhrh	rhrh	=	50% Rhrh	50% rhrh		
3.	RhRh	rhrh	=	100% Rhrh			
4.	Rhrh	Rhrh	=	25% RhRh	50% Rhrh	25% rhrh	
5.	RhRh	Rhrh	=	50% RhRh	50% Rhrh		
6.	RhRh	RhRh	=	100% RhRh			

Table I presents the Mendelian inheritance of the Rh factor which is a dominant characteristic. RhRh represents a condition in which similar genes have been derived from both parents and the individual is duplex (homozygous) as regards the character. Rhrh represents a condition in which the individual has received the gene from only one parent and is therefore simplex (heterozygous) with regard to the character; half of the gametes of such an individual will have the gene and half will lack it. Lastly rhrh represents absence of the factor and such an individual is nulliplex (Rh negative). He or she will not have the gene represented in any of the gametes and cannot, of course, transmit a trait represented by it.<sup>7</sup> We shall attempt to designate into which class each family group that we have analyzed will fall.

## CASE 1.—

Father Rh positive *Rhrh	+	Mother Rh negative rhrh	=	First Twin Rh-negative male 50% rhrh	+	Second Twin Rh-positive female stillborn 50% Rhrh
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The second twin we assume was Rh plus because of its typical hydrops. It is unusual to encounter erythroblastosis where a mother has not been previously sensitized by transfusion or pregnancy.

Levine has stated that the capacity to produce anti-Rh agglutinins differs in individual subjects so that in some women the first pregnancy may result in an erythroblastotic infant.<sup>4</sup> There is the speculative possibility that the blood of the surviving twin also produced antibodies which hastened the demise of its womb mate. Levine has also stressed the importance of determining the homo- or heterozygosity of the male parent in prognosticating the patient's percentage chance of having a normal (Rh-negative) child once she has become sensitized to the Rh factor.<sup>8</sup> In the above case the chance in future pregnancies will be one in two.

## CASE 2.—

Father Rh positive *RhRh		Mother Rh negative rhrh	=	First Twin Rh-positive male 50% rhrh		Second Twin Rh-positive male stillborn 50% Rhrh
			or			
RhRh		rhrh	=	100% RhRh		

\*Refers to Mendelian group in Table I.

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## CASE 5.—

Father	Mother	First Child	Twins
Rh positive *Rhrh	Rh positive Rhrh	Rh positive female 25% RhRh	Rh negative male Rh negative male 50% Rhrh 25% rhrh

The twin pregnancy in Case 5 was preceded by the delivery of a normal female two years before. The second twin was a normal boy now six months old. The first was a male weighing 6 lb., 11 oz. The head was large with wide sutures and fontanelles. Respirations were poor and the skin was very pale. Beginning on the second day there was some dark red bleeding from mucous membranes. He continued poorly and died eleven days after delivery. Unfortunately an Rh determination was not done and we have placed the child in his brother's Rh category because the pregnancy was monochorial. The diagnosis at autopsy was immaturity. There was no evidence of intracranial hemorrhage. However, in view of the anemia, bleeding from mucous membranes, we believe this child's condition might be logically explained by the presence of an Hr factor. Levine<sup>4</sup> has demonstrated the presence of anti-Hr agglutinins in the blood of Rh-positive mothers of Rh-negative children who showed erythroblastosis. We have had both an Rh-positive infant of an Rh-negative mother and a negative infant of a positive mother who were well at birth and between the third and fourth days developed melena. Both were promptly controlled by transfusions of Rh-negative blood and withdrawal from breast feeding.

## CASE 6.—

Father	Mother	First Child	Second Child	Twins
Rh positive Rhrh	Rh positive Rhrh	Rh-positive male 25% RhRh	Rh-positive female 50% Rhrh	Rh-negative male Rh-negative male 25% rhrh

Two normal children preceded the twins. The third pregnancy was uneventful. Labor began at thirty-five weeks and was quite easy. The first infant was a 4 lb., 10 oz. male who survived a feeding problem and is now 6 years old. The second was a 5 lb., 7 oz. male who was pale and apneic at birth, and died thirty-six hours later. Autopsy revealed an intradural hemorrhage and atelectasis. We have seen a fatal intracranial hemorrhage in the second child (Rh positive) of an Rh-negative mother and an Rh-positive father. It could be coincidence, but it seems reasonable to assume that intracranial bleeding is as likely to result from hemolytic disease as is bleeding in other areas. The above case could be explained by an Hr factor, as was Case 5.

We feel that further study and prolonged observation will reveal the Rh or other blood factors as the offenders in conditions whose explanations as such seem illogical at present. Levine has pointed out that the distribution of the Rh factor is limited to the red blood cells. In view of this, is it not illogical to speculate on the part that agglutinins may play in the production of fetal abnormalities such as hydrocephalus, anencephalus, spina bifida, amputation of extremities, etc.? And yet we have noted, as have many others<sup>9, 12</sup> the higher incidence of such conditions in families with proved parental Rh incompatibility.

## Summary

1. A series of multiple pregnancies has been studied.
2. Six cases which clinically and serologically suggested Rh incompatibility have been investigated and discussed in detail.

\*Refers to Mendelian group in Table I.

out the fact that there was a long interval—four to six years—between the finding of the early lesions in the biopsy and the appearance of clinical cancer.

In 1938 Stevenson and Seipiades<sup>8</sup> reported 18 cases of noninvasive carcinoma. Two of these cases went on to invasive carcinoma. In one of these there was a period of eight and one-half years from noninvasive changes in the surface epithelium to definite clinical cancer. The other case showed microscopic invasion of the stroma after three years.

A study of 406 cases of carcinoma of the cervix by Knight<sup>9</sup> in 1943 yielded 17 early, superficial lesions. It was believed that these lesions developed slowly, and not infrequently arose in tissue which had undergone squamous metaplasia.

In 1944 TeLinde and Galvin<sup>10</sup> reported 11 cases of early carcinoma of the cervix. In these cases biopsy revealed surface changes typical of carcinoma. Removal of the cervix followed by serial sectioning showed areas of invasive carcinoma in 10 cases. A second biopsy showed invasive carcinoma in the eleventh case. This report demonstrates the definite relationship of surface carcinoma to invasive carcinoma. It emphasizes the fact that, although a biopsy may only show surface carcinoma, serial sectioning of the cervix will often reveal areas of definite invasion.

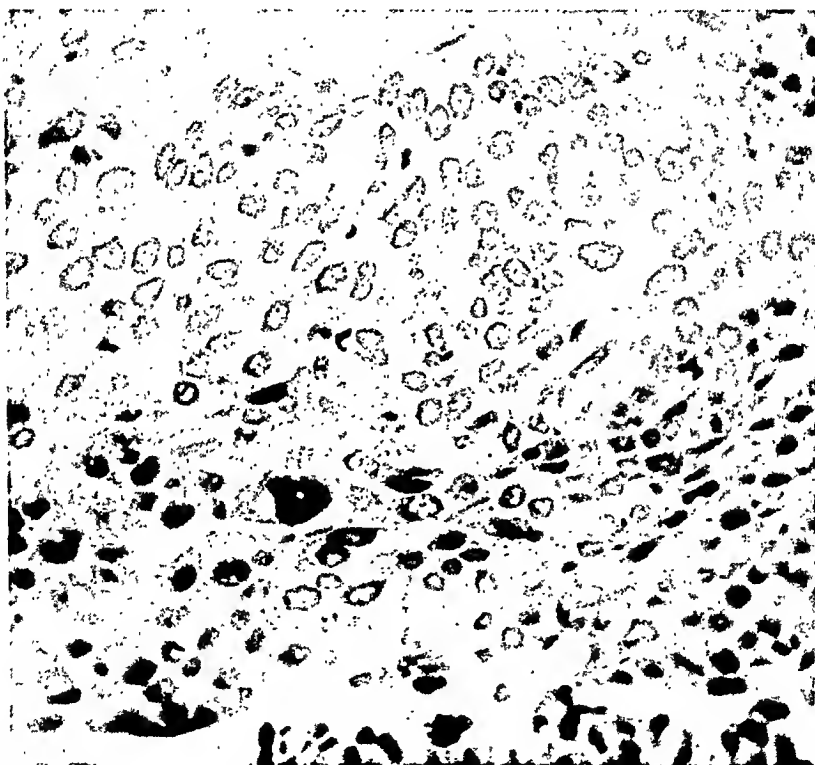


Fig. 1.—Pre-invasive carcinoma unrecognized in the biopsy of 1938. ( $\times 536$ .)

### Case Report

The patient of this report (M. M.) was a 50-year-old white, married, Irish woman. Her past history was irrelevant, except for one full-term pregnancy and a spontaneous abortion at four months. There was no familial history of cancer.

In 1932, at the age of 37 years, she accidentally discovered a lump in her right breast which proved to be a carcinoma. A radical mastectomy was performed in November, 1932, and the pathologic report was "carcinoma of breast, probably of duct cell origin." The lymph nodes showed no metastases. She

## A SEVEN-YEAR HISTORY IN EARLY CERVICAL CANCER

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THE natural history of cancer of the cervix during its clinical stages is fairly well known, but that of the early phases of its development has largely escaped observation. Evidence has recently appeared suggesting that many months, perhaps years, may elapse before a beginning cancer, detectable only on microscopic examination, attains a size to permit clinical recognition. The possibility of a successful program of prevention may well depend on the proof that such a long preclinical stage is of regular occurrence.

A case recently seen on the Gynecological Division at Bellevue Hospital reveals such a long preclinical stage. Through a failure to recognize the histologic features of an early cancer of the cervix in a biopsy obtained in 1938, a patient was allowed to proceed without specific treatment for the carcinoma until 1945, at which time the disease had progressed to a readily recognizable, but still early clinical stage. The case is important in that it illustrates several of the changing concepts of cervical cancer.

The symptoms of carcinoma of the cervix were formerly described as three in number, namely, bleeding, discharge, and pain. These are, however, the symptoms of fully developed, usually advanced, cancer. It is now evident that there may be no symptoms of early carcinoma of the cervix. Only regularly repeated, routine pelvic examinations will permit the recognition of even a majority of the cases in an early stage.

A comparable change has occurred in the concept of the pathologic diagnosis of carcinoma of the cervix. Many gynecologic pathologists have attempted to recognize earlier lesions than the fully developed invasive type of carcinoma. Perhaps the first description of carcinoma when still confined to the surface epithelium is that of Schottlaender and Kermanner,<sup>1</sup> who, in 1912, noted that the edge of an invasive growth had replaced the surrounding surface epithelium much like the icing on a cake.

In 1912 Bowen<sup>2</sup> described a comparable lesion of the skin which microscopically was confined to the epithelium and showed hypertrophy of the horny and proliferation of the Malpighian layers, mitoses, nuclear clumping, and cell vacuolization. It is found on skin and mucous membranes such as the vulva, vagina, upper respiratory and alimentary tracts,<sup>3</sup> and even the cornea.<sup>4</sup> In 40 per cent of the mucosal cases actual clinical cancer results. Metastases may occur with little change in the original lesion and minimal infiltration downward, or an atypical squamous-cell carcinoma with infiltration of the connective tissue may occur.<sup>5</sup> It appears then that carcinoma can occur microscopically and clinically with no local tissue infiltration.

In 1933 Schiller<sup>6</sup> reported a case of carcinoma of the cervix which microscopically showed carcinoma cells confined to the epithelium except for two small areas of downward penetration. This carcinoma was found following a total hysterectomy. Four years later the patient developed clinical carcinoma, probably from a small metastatic growth.

In 1934 Smith and Pemberton<sup>7</sup> presented 16 cases of early carcinoma of the cervix, including some cases of noninvasive carcinoma. These cases brought



which did not stain with iodine. A biopsy was taken. The first pathologist who saw the slide made a diagnosis of "epithelioma—transitional cell type." The slide was then reviewed by a second pathologist who did not feel that sufficient tissue was present to justify a diagnosis of carcinoma. Another biopsy was taken which was reported as chronic cervicitis. In May, 1938, a supra-cervical hysterectomy and bilateral salpingo-oophorectomy were performed on the Gynecologic Service at Bellevue Hospital. The pathologic report from the material obtained was "multiple fibroids of the uterus, atrophic uterus, normal tubes and ovaries."

Following operation the patient returned every six months, but repeated speculum examinations showed the cervix to be apparently normal. In February, 1945, a proliferating, nodular erosion of the cervix was seen. The parametria were clear. A biopsy of the cervix was taken and showed "squamous-cell carcinoma with invasion." Radiation therapy was immediately started, with the case classified as in Stage I.

The original slides obtained in 1938 were then reviewed. Despite the small amount of tissue, it was now agreed that there was sufficient variation in size, shape, and staining properties of the squamous cells to justify a diagnosis of carcinoma. The cell changes were confined to the epithelium (Fig. 1). The paraffin block was then completely sectioned. In several slides, in addition to the above cell changes, there were small invasive tongues of abnormal squamous cells extending into the fibrous stroma (Fig. 2). Fig. 3 shows the fully developed invasive carcinoma from the biopsy of February, 1945.

### Discussion

This case embodies several controversial aspects in the present concept of cervical cancer and its management.

The long time which may elapse between the origin of the early lesion in its microscopic form and the possibility of clinical recognition is the most striking point. In this case seven years passed between the original biopsy which showed microscopic carcinoma and the proliferating nodular erosion of the cervix. This observation is similar to some of the cases reported by Schiller<sup>6</sup> and Smith and Pemberton.<sup>7</sup>

It appears that cancer of the cervix may be latent for years. Later the growth appears to be accelerated, and the cancer becomes infiltrative. Whether this is a true change in the rate of cellular proliferation under the influence of some unknown stimulus, or the increase in rate is only apparent, and due simply to the cumulative effects of cell division in geometric proportion, is not clear.

Disagreement in the interpretation of these early lesions already exists and may become intense as the importance of correct evaluation becomes more widely recognized. Pathologists are uncertain as to the justification of labelling a lesion as carcinoma when it is confined to the epithelium. Some believe these lesions may become carcinoma or are to be regarded as precursors of carcinoma<sup>11</sup> (Stevenson<sup>8</sup>); others feel that carcinoma is carcinoma from the start and should be considered and treated as such<sup>7, 12, 13, 14</sup> (Scipiadès<sup>9</sup>). Correct concepts and accurate diagnoses are essential if the two dangers of delay, on the one hand, and excessively radical surgery on the other are to be avoided.

The case just reported is evidence in favor of complete as opposed to supra-vaginal hysterectomy whenever the cervix is at all abnormal. If a total hysterectomy had been done for this patient in 1938, it is quite probable that the entire tumor would have been removed. Cervical stump carcinomas amount to 3 to 4 per cent of all carcinomas of the cervix. As in this case, many carcinomas are present at the time hysterectomy is done for other reasons and are only recognized later.<sup>15</sup> Unless there is great technical difficulty involved, total

was given several courses of postoperative x-ray therapy, and in early 1933 x-rays to the pelvis for suppression of the ovarian function. The patient returned for periodic examinations, and in April, 1938, a vaginal examination was performed. The uterus was found to be enlarged and irregular in shape. A small erosion was noted on the right side of the cervix

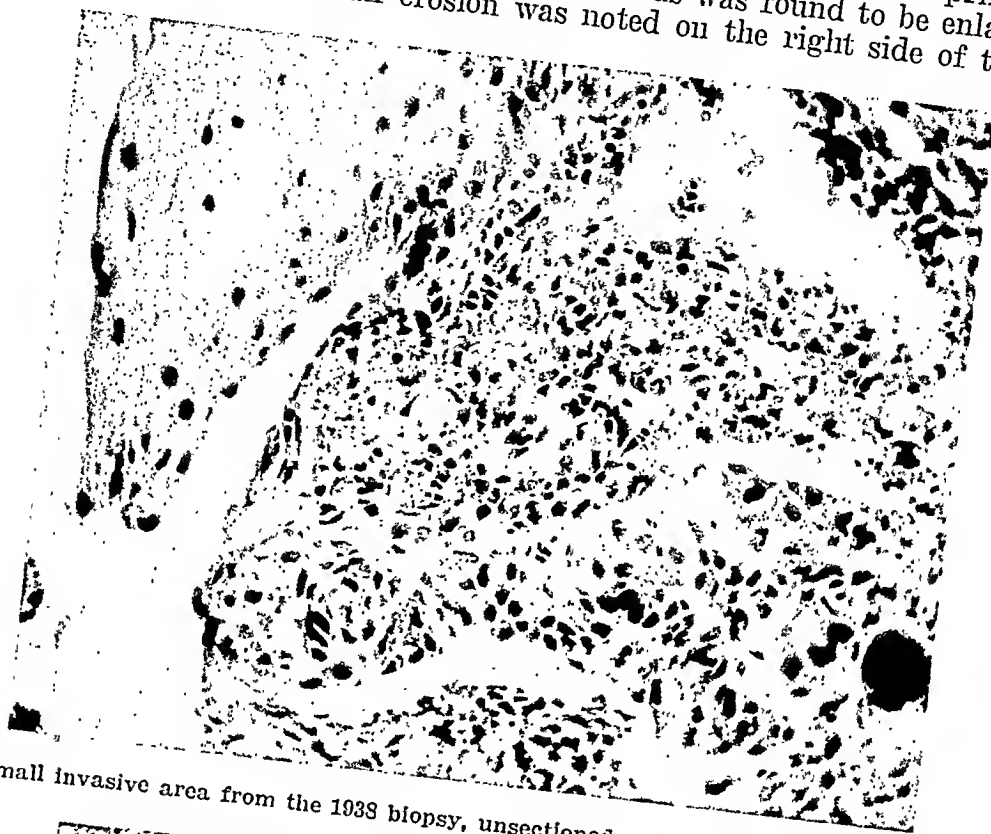


Fig. 2.—Small invasive area from the 1938 biopsy, unsectioned until later review of case. ( $\times 386$ .)

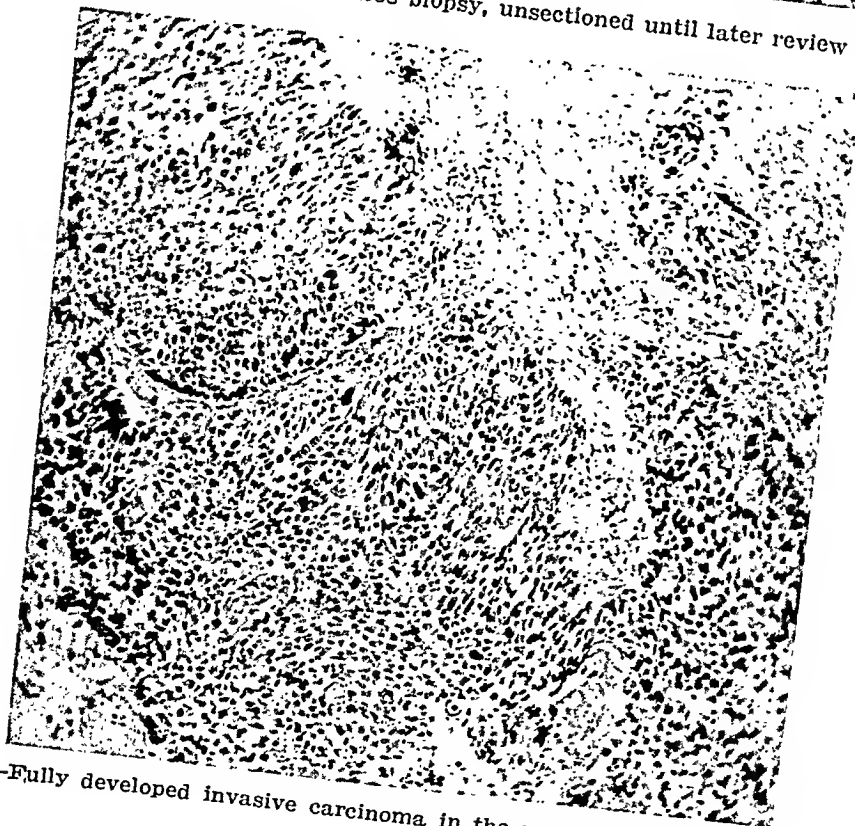


Fig. 3.—Fully developed invasive carcinoma in the new biopsy of 1945. ( $\times 134$ .)

## RETROPERITONEAL TUMORS SIMULATING GENITAL TRACT NEOPLASMS

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RETROPERITONEAL tumors are almost clinical and pathologic curiosities. Gynecologists with considerable surgical experience are rarely confronted with these abnormalities. Yet, with occasional exception of the general surgeon and urologist, these tumors, because they frequently lie in or near the pelvis, come to surgery in our field. The diagnosis is often difficult to establish preoperatively, and in our experience the growth is usually mistaken for ovarian and uterine tumors. Because the literature on this subject is sparse, and having a recent example presenting unusual features, we feel that the subject and case are worthy of review.

Tumors of the mesentery are believed by many to have a common origin with retroperitoneal tumors in the mesenchyme surrounding the primitive coelomic cavity. The pathologic conditions resulting therefrom are of wide variety. The tumors may be cystic or solid, benign or malignant. They are derived from: (1) retroperitoneal organs and their anlagen; or (2) retroperitoneal connective tissues. A review of the literature on the subject fails to give us a complete outline of this tumor group. The following classification of retroperitoneal and mesenteric tumors is therefore proposed.

The commonest cystic tumor, according to Moore, is a lymphatic cyst; and the most frequent solid tumor, the lipoma. Hinton agrees that the lipoma is most frequently found. Ewing and others are of the opinion that the existence of retroperitoneal dermoids and Wolffian cysts is quite rare. Hinman and co-workers, in 1924, were able to find only four cases of Wolffian or mesonephric cysts reported in American literature. Experience differs regarding the degree of malignancy. In one series of 22 cases reported by Rankin and Major, there were eight cases of sarcoma. Our experience, however, is that of a much lower incidence of malignancy. A likely factor in explaining this discrepancy is the rarity of surgical intervention for such tumors. Consequently, no large series is available for study.

In the previous twelve years, 13,113 gynecologic operations have been performed here in the Woman's Clinic of the New York Hospital. Yet, during this time we could find only 12 cases of retroperitoneal tumor, giving an incidence of 1:1,093. Table II summarizes these cases.

Our patients were largely of the middle age group, although postmenopausal ages were also included. It is interesting to note that in four instances the correct location of the tumor was made preoperatively; in the other cases the tumor was thought to be of ovarian or myomatous origin. The symptoms were not pathognomonic and were not uniformly present.

hysterectomy is the procedure of choice in lacerated and eroded cervixes, and probably in routine cases. Morbidity rates in the hands of trained operators are no higher in total abdominal hysterectomy than in other types of hysterectomy.<sup>16</sup>

The case illustrates finally the need of constant care in all medical phases if cancer of the cervix is to be detected early. The repeated vaginal examinations at six-month intervals made it possible, in spite of an originally erroneous pathologic diagnosis, to recognize this cancer before it had progressed beyond the cervix. The need of meticulous laboratory work is shown by the fact that only after serial sectioning of the tissue blocks of the original specimen was it possible to demonstrate the small tongues of invasive carcinoma. Surface carcinoma in one portion of a lesion does not exclude invasive changes in other parts.

### Summary

A case of early carcinoma of the cervix with minimal histologic invasion by biopsy is presented. Seven years following the biopsy clinical carcinoma developed. A review of the literature is presented, and the problems of early diagnosis are discussed.

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### Case Report

Mrs. C., a 57-year-old married woman, was admitted to the Woman's Clinic of the New York Hospital because of the presence of a huge abdominal tumor. Since delivery of her last child seventeen years ago, she had noted some swelling of her abdomen. More definitely in the last five years there had been a progressive enlargement. Her family physician was consulted three years ago. On finding the tumor which he considered an ovarian cyst, he advised operation. The patient, however, refused his advice and refused further medical care until this present admission. Because of the tremendous size of the tumor, the patient was unable to be ambulatory, and had consequently been bedridden for the past eighteen months. Further enlargement of the tumor in the last year not only confined the patient to bed, but prevented her from turning; she had lain constantly on her left side.



Fig. 1.—Mrs. C. Abdominal protrusion from huge retroperitoneal tumor. Photograph taken on admission.

She presented few complaints other than those relevant to the size and weight of the tumor. There was soreness and some pain in the skin of the left side of her abdomen and thighs; this was due presumably to the excoriation and secondary infection.

She had no systemic symptoms. Her bowel habits were regular and her appetite was fair. Menopause at the age of 50 years was not disturbing, and there had been no postmenopausal bleeding.

TABLE I. RETROPERITONEAL AND MESENTERIC TUMORS

I. Cystic Tumors	
A. Neoplastic and infectious	
1.	Dermoid cyst
2.	Pseudomucinous cyst
3.	Parasitic and inflammatory cysts
4.	Pyelonephritic abscess
B. Developmental and congenital	
1.	Wolffian cyst
2.	Chylous cyst
3.	Serous inclusion cyst
4.	Cysts of kidney, adrenal and pancreas
5.	Congenital and acquired hydronephrotic kidney
6.	Ventral meningocele
C. Traumatic sanguineous cyst	
II. Solid Tumors	
A. Benign	
1.	Mesenchymal connective tissue tumors, e.g., fibroma, lipoma, neurolemmoma
2.	Benign tumors of the adrenals
B. Malignant	
1.	Mesenchymal sarcomas, e.g., fibrosarcoma, liposarcoma, Hodgkin's disease
2.	Teratomatous adenocarcinoma
3.	Carcinomas of kidney, adrenal and pancreas
4.	Sarcoma of the kidney (Wilm's tumor)

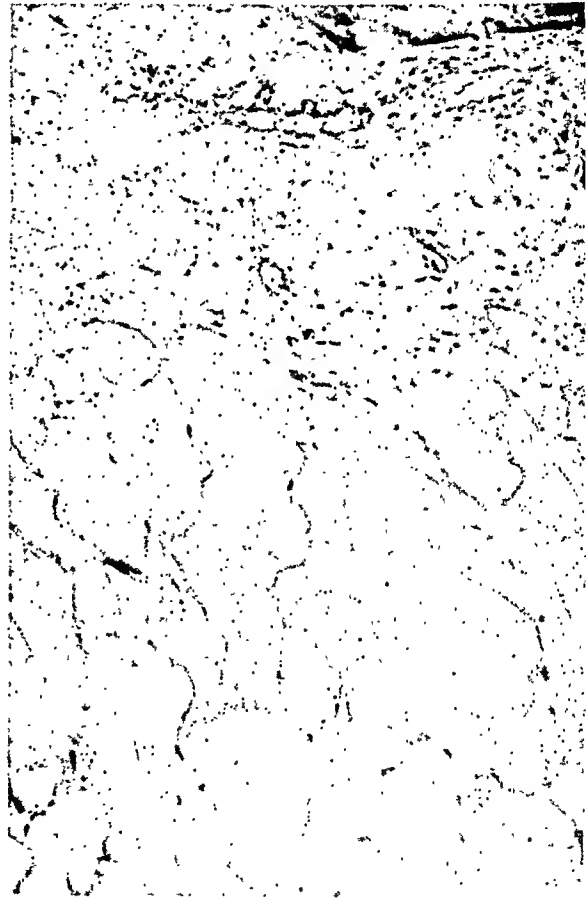
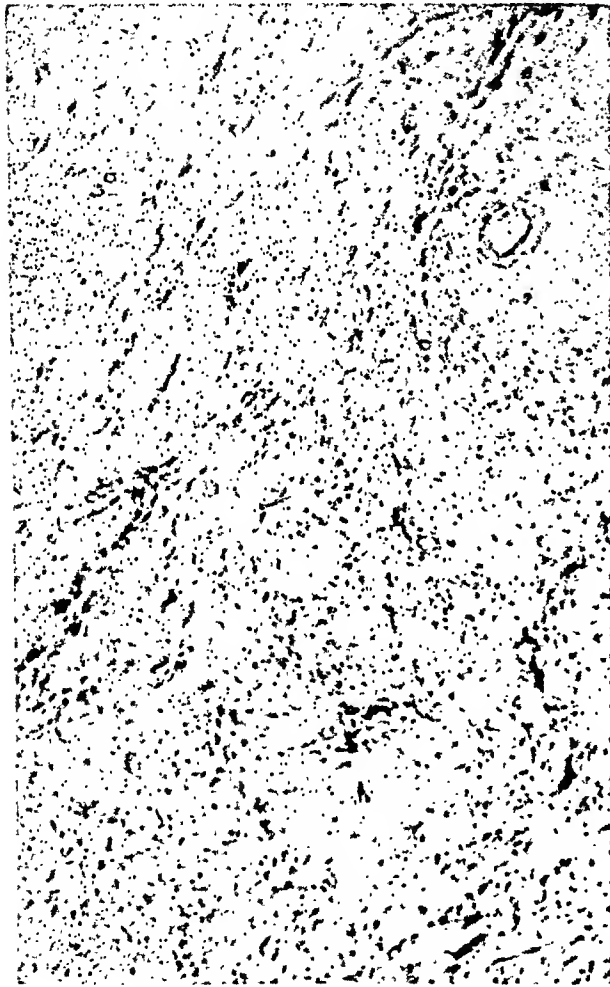
TABLE II. RETROPERITONEAL TUMORS

NO.	NAME	HOSPITAL NUMBER	AGE	PREOPERATIVE DIAGNOSIS	SYMPTOMS	PATHOLOGIC DIAGNOSIS
1.	M.L.	118268	46	Myoma uteri	Feeling of weight in the pelvis	Retroperitoneal fibroma
2.	A.M.	195924	41	Ovarian tumor	Abdominal mass and discomfort	Tuberculous pyelonephrosis of kidney
3.	V.N.	216125	20	Ovarian cyst	None	Retroperitoneal pseudomucinous cystadenoma
4.	M.S.	28754	36	Retroperitoneal cyst	Abdominal mass	Retroperitoneal dermoid cyst
5.	J.L.	201639	57	Retroperitoneal tumor	Abdominal mass	Retroperitoneal lipoma
6.	D.F.	229747	27	Retroperitoneal tumor	None	Retroperitoneal cyst of Wolffian duct origin
7.	E.G.	278206	31	Retroperitoneal tumor	Abdominal pain	Retroperitoneal neurolemmoma
8.	T.C.	174612	30	Ovarian cyst	None	Retroperitoneal cyst of Wolffian duct origin
9.	D.C.	361768	57	Ovarian cyst	Abdominal mass	Retroperitoneal myxofibroma
10.	C.S.	407280	33	Ovarian tumor	Back pain	Congenital hydronephrotic kidney
11.	M.M.	299509	65	Myoma uteri	Nausea and vomiting	Adenocarcinoma of the cul-de-sac, probably teratomatous in origin
12.	E.N.	436854	46	Enterocoele	Vaginal protrusion	Retroperitoneal fibrosarcoma

All tumors were benign with the exception of the last two.  
Patient No. 11 died of recurrence two years later.

Our interest was focused on this subject recently through the handling of a rather unusual case of retroperitoneal myxofibroma. Because of the rarity, in recent years, of huge abdominal tumors, they have become medical curiosities in diagnosis and surgical treatment.

and the tumor was gradually mobilized by blunt and sharp dissection out of the pelvis and finally away from its broad abdominal base. Following its removal, 6 Gm. of sulfanilamide powder were sprinkled in the retroperitoneal and intraperitoneal cavities. Before final closure, inspection revealed a perforation of the abdominal wall on the side opposite the original incision and underlying the tumor. This rent was closed from within with chromic catgut. The edge of the parietal peritoneum overlying the site of the tumor was united and the anterior abdominal wall closed in layers. During the course of the operation the patient was transfused with 1,900 c.c. of blood. Her condition remained fair throughout most of the four-hour procedure, but became precarious at the time of the abdominal closure. For this reason no attempt was made at the time to excise the redundant anterior abdominal wall.



Photomicrographs of retroperitoneal myxofibroma and Eosin stain. ( $\times 90$ .)

Fig. 3.—Section shows a varied cellular structure of benign fibroma.

Fig. 4.—Section is through an area of myxomatous tissue with relatively loose areolar pattern, scattered spindle-shaped cells, and precipitated mucin.

The tumor was found to weight 59 pounds. Pathological report by Dr. Marchetti was as follows:

“This is a tremendously enlarged multilobular semisolid tumor. It consists of two large divisions which are connected by a pedical 10 cm. in diameter. The over-all dimensions are 14 by 48 by 58 cm. The consistency of the tumor is soft, but for the most part it is solid. The capsule is not penetrated by any

The striking physical findings on admission were limited to the abdomen. It was tremendously enlarged by the presence of a tumor which at the time was thought to be semisolid and nodular. The huge tumor caused the abdomen to protrude to the extent that it required the separate support of a wide hospital bed. The abdominal mass measured 100 by 60 by 20 cm. No fluid wave could be elicited. The overlying skin on the left side of the abdomen, groin, and inner aspect of both thighs was extensively eroded and secondarily infected.

Pelvic examination disclosed a healthy cervix. The uterus and adnexa were drawn up out of the pelvis by the tumor and could not be palpated. Physical findings were not otherwise remarkable save for emaciation and evidence of weight loss. Supporting measures consisting of wet saline compresses to the excoriated skin, fluid replacement with parenteral administration of vitamins, and transfusions were instituted. During the first twenty-one days temperatures ranged to 38° and 39° C.



Fig. 2.—Mrs. C. Thirty-ninth hospital day. Note beginning healing of skin and healthy granulation overlying large abdominal mass.

Her preoperative course thereafter was essentially afebrile. In the seventy-nine day period she received eight transfusions, totaling 4,000 c.c. of citrated blood, bringing the preoperative hematocrit to 41 per cent, with a hemoglobin of 11.3 grams. Sulfadiazine, 6 Gm. daily, was administered prophylactically during the seven days immediately prior to operation. During the three-month period of hospital rest there was gradual improvement in her general health, and in the granulation and partial epithelization of the eroded skin of the abdomen and thighs. Various methods and medications for improving the condition of the skin were tried; none seemed specific. X-rays taken of the abdominal protrusion revealed the presence of a segment of bowel in the mass.

Her condition was finally thought satisfactory for operation, and on the seventy-ninth hospital day she was operated on by the authors, under open drop ether anesthesia. A lower right rectus incision was made over the protruding abdominal mass. Sterile drapes had previously been applied to the under surface of the abdomen to exclude the area of persistent skin erosion. On entering the abdominal cavity the pelvic organs were found and, together with a normal-appearing bowel, were found displaced by a huge retroperitoneal tumor extending from the pelvic floor to the diaphragm, originating in the left abdominal sulcus region. The peritoneum overlying it was entered



day and one hundred sixty-fourth day after admission, the patient was in good health and had regained a weight of 104.9 pounds. The ventral herniation of approximately 8 cm. in diameter persisted.

Mrs. C. was readmitted three months later for removal of the redundant skin of the abdomen and repair of the ventral hernia. The patient was found to be in good health; she weight 129.1 pounds. Physical findings on admission were normal save for the presence of the ventral hernia and redundant skin with ulceration. The skin ulcerations were finally brought to complete healing during the 42-day preoperative period.

The patient was taken to the operating room and, under gas, oxygen, and ether anesthetic, a plastic operation on the abdomen and repair of the incisional hernia were performed. The patient tolerated well this second, relatively short operation (thirty minutes). Her course was afebrile; she was allowed up on the eighteenth and discharged on the twenty-seventh postoperative day. Final examination revealed satisfactory healing with good abdominal wall support.

She has since been seen on several occasions in the gynecologic follow-up clinic. At the time of her last visit, two years and four months after the operation, the patient was found to be in good health and weighed 164.7 pounds.

### Comment

Diagnosis of this and other cases in our series was more often wrong than right, and such has been the experience of others. We are gratified, however, that in four instances retroperitoneal origin was diagnosed preoperatively. The diagnosis is most often confused with ovarian cysts and tumors, and with myoma uteri. Under certain circumstances correct interpretation can be made beforehand. Valuable in the diagnosis is the relative fixation of the tumor to abdominal and pelvic examination. If it is not large the internal genital organs may be ascertained as separable and movable from the tumor in question. Ascites is absent.

The usual history is of importance only in excluding primary pathology in the lower bowel and uterus. If the true location of the tumor is suspected, intravenous pyelography can be very helpful in: (1) showing disturbance or absence of function when the tumor is of renal origin; and (2) showing a wide displacement of the ureter, and occasionally the kidney as well, by the neighboring retroperitoneal tumor. X-ray of the bowel tract may or may not be helpful. The crux of the diagnosis is constantly bearing in mind the possibilities of retroperitoneal tumors.

The operative approach to such tumors is usually transperitoneal through the abdomen. Lahey and Eckerson suggest also a lumbar-kidney approach in selected cases. The surgical procedure of choice will depend in the main on the type and location of the tumor.

### Summary

The subject of retroperitoneal and mesenteric tumors has been discussed. Both have common derivation in the extracoelomic mesenchyme. Lacking a satisfactory grouping encompassing all these tumors, a suggested classification

growth, but on the surface there are many large vessels included in the capsule. The cut surface of the tumor shows a pearly-white myxomatous pattern which in some places is rather solid and undergoing calcareous degeneration. In the smaller more dependent lobules the tissue is more myxomatous.

"Microscopic section through the tumor shows the substance to be of rather loose texture. It has a myxomatous appearance, and the small nucleated spaces are supported by cells which are spindle shaped and spider shaped. There are many small blood vessels, and here and there some of the larger spaces are filled with acidophilic material. There is nothing in the pattern or texture of the growth which suggests malignancy. In certain areas the cells are more contiguous and appear to be of fibrous origin. The polychrome stain shows that, aside from the fibrous connective tissue, there are areas in which one also finds a few strands of muscle tissue. Additional microscopic sections show tumor tissue as described above, and also show scattered areas of hyalin degeneration and deposits of calcium salts. The diagnosis is myxofibroma, retroperitoneal."

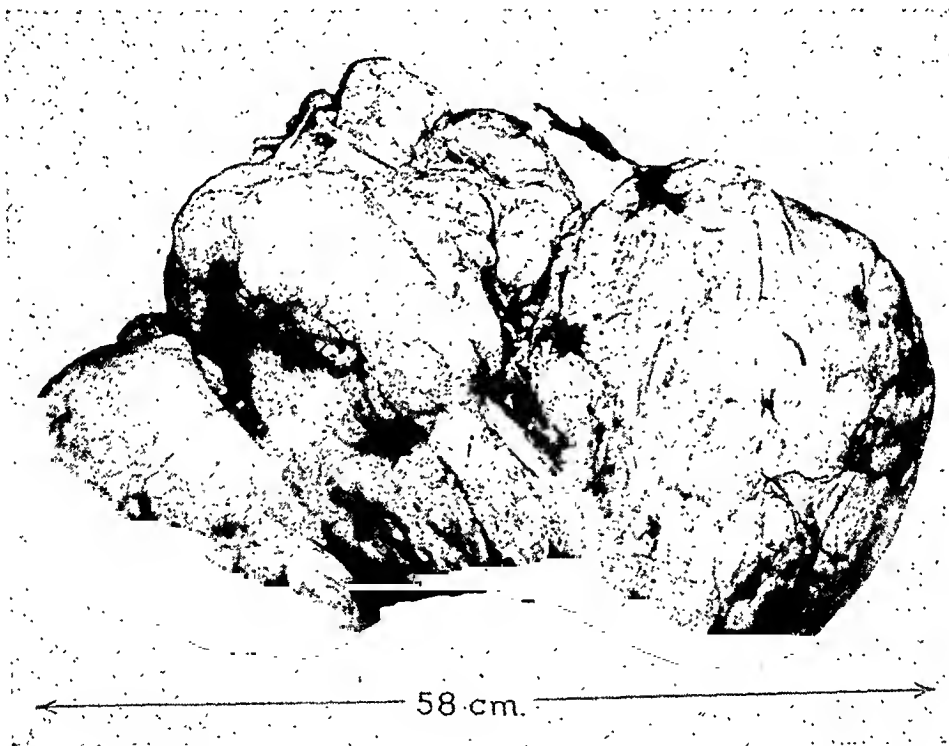


Fig. 5.—Huge retroperitoneal myxofibroma. Tumor was pearly white and of soft myxomatous consistency; weight, 59 pounds.

The patient's postoperative course was stormy and febrile for fifteen days. During this time she received an additional 2,500 c.c. of blood, parenteral hypertonic fluid, and sulfadiazine totaling 50 grams. Oxygen by tent and continuous duodenal suction were required for the first five precarious days. Her course steadily improved. The patient was out of bed on the thirty-sixth postoperative day (the first day up in twenty-seven months). On the fifty-second postoperative day she weighed 81.2 pounds, which was less than one-half her usual weight.

The abdominal incision healed by secondary intention. The original extensive skin erosion of the abdominal wall had shrunk to two small areas of healthy granulation. At the time of discharge, on the eighty-fifth postoperative

## TORSION OF ADNEXAL TUMORS AND ITS RELATION TO SURGICAL EMERGENCY

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**T**ORSION of the pedicle is probably the most common complication of non-inflammatory adnexal tumors. According to certain gynecologists, it occurs in 10 to 20 per cent of such lesions, even though it is rarely marked enough to produce symptoms per se, but is discovered during surgical intervention aimed at removal of the recognized tumor. On the other hand, it is commonly considered that a twisted pedicle which is producing definite symptoms constitutes an emergency requiring immediate operation. This study was undertaken to test the validity of the latter view.

Between July 1, 1926, and Dec. 31, 1940, among 13,505 obstetric and 12,991 gynecologic admissions to the University Hospitals, there were 42 instances of adnexal tumors with symptom-producing torsion of the pedicle. Three cases appeared among the obstetric patients (1:4,501), and 39 in the gynecologic group (1:333). No patient was included in the series unless the torsion was at least 180 degrees. All clinical diagnoses of "torsion" were substantiated at operation, but all torsions were not diagnosed preoperatively.

The age incidence (Table I) was not remarkable, except perhaps for its even distribution. The youngest patient (aged 13 years and prepubertal) had a twisted hydatid of Morgagni about the size and color of a cherry, which produced acute symptoms.

Thirteen patients had never been pregnant, while 29 were either pregnant at the time or had had from one to several children. The three pregnant women who had gestations of  $3\frac{1}{2}$ , 4, and 5 months, respectively, continued to full term and were delivered spontaneously.

One patient had not reached puberty, and 17 were postmenopausal. Among the other 24, menstruation was normal except for menorrhagia in two (aged 18 and 51 years, respectively) and dysmenorrhea in eight (severe in only one).

Ten patients had been subjected to previous pelvic or abdominal surgery: appendectomy without drainage, eight; dilation and curettage, two; cervical polypectomy, one; vaginal plastic repair, one; and uterine suspension, one. Two women had been delivered four to six weeks before admission when they presented tumors as large as full-term pregnant uteri.\*

Each patient was able to indicate the development of the first symptom of torsion to her state of activity at the time: 35 were on their feet, six were asleep, and one was sitting quietly. The onset was sudden in 23, and more gradual in 19. A history of previous similar attacks was elicited from 14 women, with relief after varying periods, but without surgical intervention.

The most common symptoms (Table II) were pain, tumor, nausea, and vomiting, with their severity seemingly proportional to the suddenness of the attack. The interval between the appearance of the first symptom and examination at the hospital averaged approximately one year, with extremes of sixteen years and eight hours (Table III). In some instances, symptoms

\*Reported by E. von Graff, J. Iowa M. Soc. 25: 118-124, 1935. (Cases 3 and 4.)

is proposed. Twelve cases from our records (an incidence of 1:1,093) are tabulated. Of unusual interest is one of our cases with a large retroperitoneal myxofibroma weighing nearly as much as the patient. This case is reported in detail. The diagnosis of these tumors is usually incorrect and is most often confounded with ovarian and uterine tumors. Correct differential diagnosis, in some cases possible as attested by four of ours, can be made on the basis of discriminatory examination. It is greatly aided by intravenous x-ray pyelography.

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tumor could be felt only on bimanual examination, and in one (hydatid of Morgagni) no enlargement of the adnexa was noted, and the laparotomy was of an exploratory nature. Clinical enlargement of the uterus was noted five times, including the three patients who were pregnant.

Mild to moderate leucocytosis was the rule, although a few patients with chronic symptoms had normal white blood-cell counts. The highest value was 19,000, the lowest 5,900, and the average 9,800. The highest preoperative temperature (oral) was not above 99° F. in 19 patients, between 99 and 100° F. in 12, and above 100° F. in 11. Other laboratory findings were not clinically significant.

TABLE V. FINDINGS AT OPERATION

None of the tumors was ruptured

1. Size of tumor			
a. Up to size of an orange			7
b. Orange to size of grapefruit			20
c. Larger than a grapefruit			15
2. Consistency of tumor			
a. Cystic	35		
b. Solid	7		
3. Color of tumor			
a. Black	12		
b. Dark red	8		
c. White	5		
d. Pink	4		
e. No note	13		
4. Adnexa involved			
a. Right	25 cases (60%)	{ Torsion to right { Torsion to left { No note	11 6 8
b. Left	17 cases (40%)	{ Torsion to right { Torsion to left { No note	3 8 6
5. Degree of torsion			
a. $\frac{1}{2}$ to 1 turn	24		
b. 1 to 2 turns	8		
c. 2 to 3 turns	6		
d. 3 to 4 turns	4		
6. Adhesions			
a. Absent	27		
b. Present	15		
7. Free abdominal fluid			
a. Absent		29	
b. Present		13	
		1. Bloody	5
		2. Brown	4
		3. Clear	4
8. Character of opposite ovary			
a. Normal	31		
b. Cystic	7		
c. Atrophic	3		
d. Solid tumor	1		
9. Associated gross pelvic lesions			
a. Appendix grossly pathologic		4	
b. Leiomyoma of uterus		3	
c. Pregnancy (uterine)		3	
d. Uterus enlarged (only)		2	
e. Cervical polyp		1	
f. No associated lesions		27	

TABLE I. AGE GROUP INCIDENCE

AGE GROUP (YEARS)	NUMBER OF CASES	PER CENT
10 to 20	7	17
21 to 30	9	21
31 to 40	6	14
41 to 50	7	17
51 to 60	8	19
61 to 70	5	12

TABLE II. SYMPTOMS

SYMPTOM	NUMBER OF CASES	PER CENT
Pain	30	71.0
Tumor	19	45.0
Nausea	13	31.0
Vomiting	12	29.0
Urinary frequency	8	19.0
Enlargement of abdomen	7	17.0
Heaviness in pelvis	4	9.7
Constipation	4	9.7
Loss of weight	3	7.1
Postmenopausal bleeding	3	7.1
Menorrhagia	2	4.8
Diarrhea	1	2.4

TABLE III. INTERVAL BETWEEN ONSET OF SYMPTOMS AND EXAMINATION IN HOSPITAL

Under 24 hours	2	4 months	2
3 days	3	6 months	4
4 days	3	7 to 12 months	10
7 days	2	1 to 2 years	1
1 month	4	2 to 3 years	1
2 months	3	Over 4 years	4
3 months	4		

TABLE IV. TYPE OF OPERATION

TYPE	NUMBER OF CASES	PER CENT
Unilateral salpingo-oophorectomy	10	23.8
Bilateral salpingo-oophorectomy with total hysterectomy	9	21.4
Unilateral salpingo-oophorectomy with appendectomy	8	19.0
Unilateral salpingo-oophorectomy with total hysterectomy	4	9.5
Bilateral salpingo-oophorectomy with total hysterectomy and appendectomy	4	9.5
Unilateral salpingo-oophorectomy with partial opposite oophorectomy and appendectomy	2	4.8
Bilateral salpingo-oophorectomy with subtotal hysterectomy	2	4.8
Unilateral salpingo-oophorectomy with total hysterectomy and appendectomy	1	2.4
Removal cyst of Morgagni and appendectomy	1	2.4
Unilateral salpingo-oophorectomy with appendectomy and uterine suspension	1	2.4

had been continuous but of varying severity, while in other cases there had been complete relief until the final episode.

Acute lower abdominal tenderness was the most significant physical finding, being present in 35 cases, and usually associated with muscular rigidity. Abdominal palpation revealed a mass in 35 patients, while in six others the

The histologic diagnoses on the adnexa involved by the torsion, as made by the Department of Pathology, are presented in Table VI. Because of hemorrhage and necrosis, the character of ten cystic tumors could not be determined exactly, but they were thought to be benign cystadenomas.

The microscopic diagnoses on other structures removed are shown in Table VII, and need no comment.

### Summary and Conclusions

1. Forty-two cases of noninflammatory adnexal tumors with torsion of the pedicle confirmed at laparotomy are presented.

2. The most common symptoms were pain, lower abdominal mass, nausea, and vomiting. The onset was sudden or gradual, and the symptoms constant and severe, or mild and intermittent.

3. Pseudomucinous and serous cystadenomas, dermoids, and fibromas were most frequently encountered, but apparently any cystic or solid pedunculated mass may be involved.

4. Patients with twisted-pedicle tumors may be acutely ill or may develop a semi-chronic disability. The febrile reaction and leucocytic response are not remarkable.

5. Operation is well tolerated, and postoperative recovery is usually rapid and uncomplicated. The single fatality in this series was due to cerebral hemorrhage in a 63-year-old woman.

6. A clinical diagnosis of twisted pedicle demands operative intervention, but not as an absolute emergency. When the diagnosis is doubtful, a period of observation does not significantly increase the patient's risk.

The period of preoperative observation varied from a few hours to twenty-four days, but averaged more than two days. Except in rare instances, the condition was not considered an acute emergency, and operation was scheduled in the usual manner.

The type of operation varied considerably according to the character of the primary lesion and of associated abnormalities (Table IV). The ovary on the side opposite the adnexa which had undergone torsion was removed in 15 cases, always in connection with hysterectomy. Removal of the uterus was carried out only for specific lesions (fibromyomas) or in women past the menopause.

Specific findings at operation are listed in Table V. The incidence of tumors larger than a grapefruit (35.4 per cent) may be significant, since acute and, to a greater extent, chronic torsion with its disturbance of circulation should lead to enlargement on a mechanical basis. Attention has already been directed to the rapid growth occasionally occurring after delivery in the presence of torsion, which leads to partial circulatory obstruction. Torsion appears to occur in either direction with equal facility, but in this series the right adnexa were more commonly involved.

Postoperative therapy was not specialized, except that two pregnant women were given progesterone to maintain uterine quiet, one patient with lobular pneumonia received oxygen, and another with parametritis was given foreign protein injections and pelvic heat. Some elevation of temperature was noted in all except one patient, but only seven had fever above 102° F. at any time. The only alarming elevation (105° F.) occurred in the one woman who did not survive. This fatality involved a 63-year-old patient who died forty-eight hours after operation from cerebral hemorrhage. The nonfatal complications included two cases of defective wound healing, one of paralytic ileus, one of bronchopneumonia, and one of parametritis. The 41 surviving patients were discharged from nine to forty-one days (average, thirteen days) after operation.

TABLE VI. PATHOLOGIC DIAGNOSES OF INVOLVED ADNEXA

DIAGNOSIS	NUMBER OF CASES	PER CENT
Undetermined cystic mass with hemorrhage	10	23.8
Pseudomucinous cystadenoma	9	21.4
Dermoid (teratoma)	7	16.8
Serous cystadenoma	6	14.2
Fibroma	4	9.5
Simple epithelial cyst	4	9.5
Papillary cystadenoma	1	2.4
Krukenberg tumor	1	2.4
	42	100.0

TABLE VII. ASSOCIATED PATHOLOGIC DIAGNOSES

DIAGNOSIS	NUMBER OF CASES	PER CENT
Chronic appendicitis	12	31.8
Leiomyoma of uterus	9	23.8
Follicle cysts of ovary	6	16.0
Chronic salpingitis	5	13.4
Cervical polyps	2	5.4
Krukenberg tumor (other ovary)	1	2.4
Papillary cystadenoma (other ovary)	1	2.4
Pseudomucinous cystadenoma (other ovary)	1	2.4
Endometriosis	1	2.4
	38	100.0



sediment showed occasional leucocytes and rare red cells, but was loaded with granular, hyalin, and cellular casts, and motile rods. Urine culture showed anaerobic streptococcus and diphtheroids. The urine was negative for glucose, acetone, bile, and urobilin.

Blood obtained by venepuncture:

Hemoglobin	5.5 Gm.	Color index	.59
Red cell count	3.2 million	Mean corpuscular hemo-	15.6 mm.
White cell count	29,100	globin	
Packed cell volume	21	Mean corpuscular hemo-	26.2%
Filamented polymorpho-	50	globin concentration	
nuclear neutrophil		Mean corpuscular volume	65.5 c.mm.
leucocytes		Sedimentation rate	13 corrected
Nonfilament polymorpho-	12	(Wintrobe)	
nuclear neutrophil		Mazzini	Positive
leucocytes		Kolmer	Negative
Eosinophils	4	Chlorides	637
Basophils	1	CO <sub>2</sub> combining power	(Not available)
Lymphocytes	19	Nonprotein nitrogen	39
Monocytes	8	Uric acid	8.3
Unclassified	6	Cholesterol	160
Normoblasts	30,000	Serum albumin	2.9
Anisocytosis	Marked	Serum globulin	3.6
Poikilocytosis	Marked	Icterus index	10
Sickle cells	70 per cent (standing 24 hours)		

No plasmodia on thick smear.

The clinical diagnosis was pregnancy of seven months' duration, severe pre-eclampsia, and sickle-cell anemia. The patient was placed in a dark, quiet room on a salt-free, high protein diet. Fluids were not restricted and sedation with morphine, barbiturates, and magnesium sulfate was given as indicated. Intravenous 20 per cent glucose was given slowly and with care, and nasal oxygen was given continuously. The patient received slow transfusions of 500 c.c. of blood and 500 c.c. of plasma daily on the second, third, and fourth hospital day, and blood only on her fifth day, a total of 2,000 c.c. of blood and 1,500 c.c. of plasma. The physical findings in her chest did not change significantly, and the pulse varied between 100 to 120 beats. Her fever rose to 101° F. at its peak on the second day. The hypertension remained constant at 170/110, and albuminuria increased to 7.5 Gm. per liter on her fourth day, and 14 Gm. per liter on her fifth day, though the casts decreased. Headache and dimness of vision disappeared. The hemoglobin improved to 7.6 Gm.

Since the patient had failed to respond to conservative therapy, it was decided to deliver her on her fifth hospital day. The baby was considered to be non-viable, so induction of labor by rupture of the membranes and insertion of a Voorhees bag was carried out. One and one-half hours after the insertion of the bag, without apparent reason, the patient's respirations became irregular and, within one minute, ceased. She did not respond to oxygen by mask, artificial respiration, and intramuscular coramine. The heart could not be heard after respiration ceased. The last blood pressure recorded forty-five minutes before death was 120/90, pulse 110, respirations 30. The patient was responsive and cooperative until death, and there was no sign of a convulsion. She died undelivered, with fetal heart tones inaudible at death. Clinically, death was ascribed to heart failure, with severe pre-eclampsia and sickle-cell anemia predisposing.

At autopsy the pleural cavities on both sides contained 1,000 c.c. of fluid. The lungs were partially atelectatic, but not edematous, nor were emboli or infarcts present. The heart was slightly enlarged (390 Gm.) and the right ventricle was dilated, but the myocardium looked normal. The heart and large

## SICKLE-CELL ANEMIA IN PREGNANCY

### Report of a Case With Autopsy

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SICKLE-CELL anemia is an uncommon hereditary blood dyscrasia, found primarily in Negroes and characterized by remissions and exacerbations, with exitus at an early age. Many girls with this disease die before puberty and, of those that reach maturity, many have genital hypoplasia; so that sickle-cell anemia and pregnancy are rarely associated. In 1940, Kobac and his associates<sup>1</sup> were able to collect only eleven cases from the literature when reporting six additional cases from their own experience. In fifteen of these patients the maternal mortality was 33 per cent and, of 35 pregnancies, only 51 per cent were born living. Van der Sar<sup>2</sup> has reported the case of a 26-year-old Negro woman with typical sickle-cell anemia who was observed through two pregnancies, one of which resulted in a living child. Recently, Spivaek<sup>3</sup> has reported the case of a 35-year-old multiparous Negro woman who was known to have had sickle-cell anemia for many years. This patient was successfully guided through pregnancy and puerperium without serious consequences, and a living child resulted. The rarity and seriousness of this condition warrant reporting of the following case:

S. E., a 32-year-old multiparous Negro woman, entered San Francisco County Hospital for the first time Sept. 6, 1945, with the chief complaint of headache and swelling of the ankles. She had lived in Louisiana until one month previous to entry, had never remembered being ill, though she had been told she had had malaria as a child. She had seen a doctor two months previously, who had diagnosed pregnancy but had suggested no treatment. She could not remember the date of her last menstrual period. One month before entry she began to notice dyspnea, palpitation, orthopnea, and a dry, hacking cough. About the same time she noted swelling of her ankles, fingers, and eyelids. She had had five shaking chills in the month before entry. One week before entry she noted the onset of headaches and dimness of vision, and had episodes of lower abdominal pains and occasional vomiting.

On entry the patient looked ill, and dyspnea was marked. Her temperature was 98.8° F., pulse 100, respirations 34, and blood pressure 170/100. Her face and extremities showed marked pitting edema, and she complained of headache and dimness of vision. She vomited water given her, but was alert and cooperative. The eyegrounds showed moderate "silver wire" changes and some arterio-venous nicking, but no arteriospasm, papilledema, hemorrhages, or exudates were noted. The lungs expanded equally and were clear to percussion and auscultation, save for harshness of the breath sounds. The heart did not seem enlarged, but there was a systolic thrill and murmur at the apex, and the heart sounds were labored. There was a reduplication of the mitral first sound, but no diastolic murmurs were heard, nor was the pulmonic sound unusual. The abdomen was moderately distended in the epigastrium, and the fundus rose to three fingerbreadths above the umbilicus. The fetus was estimated to weigh 1,000 Gm., and the fetal heart was audible. The liver did not seem to be enlarged or tender, but the spleen was palpable. There was no costovertebral angle tenderness. Reflexes were present, but not exaggerated.

A small volume of urine was obtained by catheter and was dark brown in color, specific gravity was 1.008, pH 6.0, albumin 4.5 Gm. per liter. Centrifuged

of pregnancy. Though we were aware of both the anemia and the sickling in the present case, and despite the fact that two staff members of this hospital have written extensively on this subject,<sup>4,7</sup> we were deceived by the clinical picture. Hypertensive toxemia is a frequently associated finding which, as in this case, may cause still further confusion.

Two unusual features of the case were the age and moderate obesity of the patient. The only older previously reported case during pregnancy was 35 years old,<sup>3</sup> and the majority of patients with sickle-cell anemia die before the age of 30 years. Usually these mothers are thin and underdeveloped. Leg ulcers were absent, and the patient had pain in her leg on only one occasion. The dyspnea, edema, cough, abdominal pains, and blood picture were characteristic. The outcome, unfortunately, was also not unusual.

In vitro studies demonstrate the characteristic change of the red corpuscles from normal to elongated sickle-shaped bodies when they are subjected to lowered oxygen and increased carbon dioxide tensions.<sup>4</sup> The pathogenesis of the disease is clearly depicted by Bauer.<sup>6</sup> The inherently defective red cells are discoid in the general circulation, but when they are subjected to lowered oxygen tension in the capillaries of organs where the circulation is slow (such as the liver, spleen, and lymph nodes) the cells undergo sickling, and congestion results. The first clinical finding is an increased tendency for thrombosis with resulting infarction or embolism. Even if actual thrombosis does not occur, the stagnation of the circulation causes ischemia, necrosis, and finally fibrosis of the viscera. The stagnant corpuscles later disintegrate, causing anemia and jaundice. In the present case the history of previous good health, the large engorged spleen, and the lack of jaundice speak for acuity of the condition. The pathologic picture indicates that this patient was suffering from a generalized ischemia due to conglutination of sickle cells in the capillaries. When in the final stage the ischemic myocardium of the right ventricle could no longer overcome the resistance of the congested pulmonary circulation, the patient died of cardiac decompensation with acute corpulmonale.

Treatment in these cases has been unsatisfactory because apparently the underlying cause cannot be altered. Transfusions seem indicated to combat anemia and are recommended by Koback, Stein, and Daro<sup>1</sup> but they seemed of little use in the present case. Probably a more gradual replacement of blood during pregnancy would be more effective, when possible, as suggested by Spivaack.<sup>3</sup> Bauer<sup>6</sup> advises physiotherapeutic measures directed at increasing the circulation through the capillaries. Page<sup>8</sup> has suggested the use of intravenous oxygen in markedly anoxic cases in hopes of retarding the sickling process, but this experiment has never been tried to his knowledge. Some cases seem to respond well to antianemic therapy with liver and iron when the acute stage is over. These patients are especially susceptible to infection, and are prone to puerperal morbidity, so that asepsis and chemotherapy are important preventive and therapeutic agents. It is hoped that more satisfactory treatment will evolve on more widespread recognition of the disease.

### Conclusions

Sickle-cell anemia is a rare but rather consistently fatal complication of pregnancy, the diagnosis of which usually is not made. Obstetricians practicing among Negroes should be familiar with the clinical picture of the disease, and be prepared for increased tendency for thrombosis and liability to fatal sepsis. In order that the diagnosis may be made before the terminal stage, the blood of all Negro mothers, or at least those showing a tendency toward anemia, should be allowed to stand in a sealed preparation for a few hours and examined for "sickling."

vessels were filled with a solid red fibrous clot. The liver was enlarged (2,030 Gm.) but appeared normal. The spleen was greatly enlarged (740 Gm.) and was dark red brown on section. The kidneys were pale, but not unusual. The fetus was a female weighing 1,130 Gm. and measuring 40 cm. The placenta was normally implanted and appeared normal.

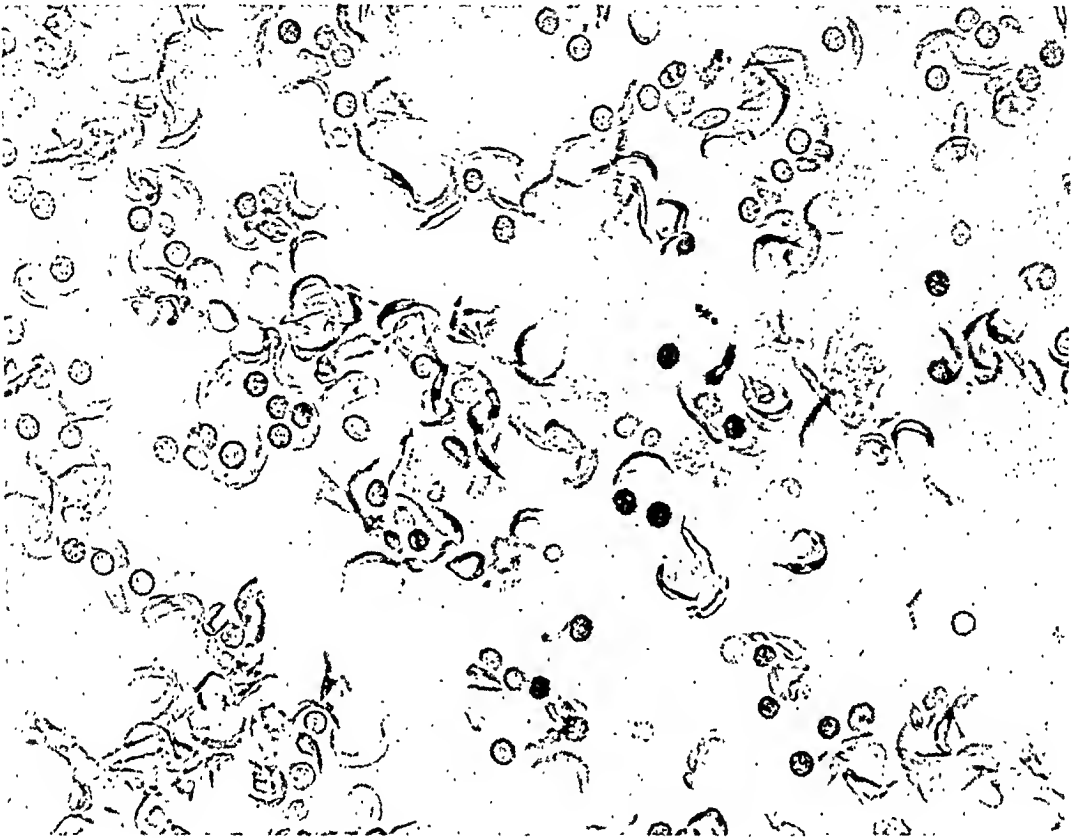


Fig. 1.

Microscopic sections showed markedly congested capillaries in all tissues, the masses of red corpuseles showing frequent sickle cells. The myocardium showed no degeneration, there was slight fibrosis of the alveoli in the lungs, normal Kupffer cells were found in the liver, and there was moderate tubular degeneration in the kidneys with albuminus exudate into the lumen. There were a very few small Malpighian corpuseles in the spleen, and the entire parenchyma was composed of red blood cells which had apparently ruptured the sinusoids. The bone marrow showed marked proliferation of the erythroblastic series and some hyperplasia of the myelocytes. No sickling was noted in the fetal blood in the placenta, but the maternal sinusoids were densely congested with erythrocytes and normocytes and many sickle cells. The pathologist reported death due to sickle-cell anemia with right-sided heart failure, pleural effusion, and visceral congestion. A clinical diagnosis of pre-eclampsia was added, though the characteristic pathology was absent.

### Discussion

Many cases of sickle-cell anemia are undoubtedly diagnosed as pneumonia,<sup>1, 4</sup> and others as rheumatic fever<sup>5</sup> until the observer becomes familiar with the syndrome. Often a case may be discovered only at autopsy.<sup>6</sup> Due to its rarity, sickle-cell anemia is seldom included in the differential diagnosis of anemia

## MULTIPLE PRIMARY CARCINOMAS

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**I**NCREASINGLY frequent reports of multiple primary carcinomas are appearing in the literature. The incidence of this formerly infrequent occurrence has also increased from 0.3 per cent to 3.7 per cent (Warren and Gates<sup>1</sup>) to 6.8 per cent (Warren and Ehrenreich<sup>2</sup>) of all carcinomas, both in surgical and autopsy material. An awareness that the current incidence figures are more than a mathematical chance, and that physicians should critically survey their primary carcinoma cases in periodic checkups for evidences of another and anatomically different carcinoma has become important.

Multiple primary carcinomas, statistically more common in males than in females, occur in an average age of 56 years. The average interval between successive tumors, as near as it can be determined, is about three years. The sites of multiple primary carcinomas in the different organs show no definite pattern, for as many combinations occur as there are organs. Slaughter<sup>3</sup> cites 15 cases in combination of the stomach and uterus out of 120 cases in which the genitourinary system and the gastrointestinal tract were involved.

It is this latter combination into which the following case report falls, and the case is of interest because of a four-and-one-half-year interval between carcinomas, and because of an apparent cure of both malignancies in an elderly woman.

Mrs. J. P., now 65 years old, white, Jewish, was admitted to the Kings County Hospital on Oct. 30, 1941, at the age of 61 years, with a history of gastric complaints over a long period of time. These included persistent vomiting, loss of weight, and an aversion to meat. An abstract of her record from the Kings County Hospital showed that a gastric resection was performed on Nov. 18, 1941, at which time the pathologic report of the surgical specimen revealed an adenocarcinoma of the stomach with ulceration. The additional discharge diagnosis also included bronchiectasis, postinfectious, instrumentation wound of duodenum, and arteriosclerotic heart disease.

A postoperative gastrointestinal series on Dec. 11, 1941, revealed evidence of a well-functioning gastroenterostomy and a small para-esophageal herniation of the cardiac end of the stomach. The patient was discharged on Dec. 14, 1941. There were no clinical symptoms from the gastrointestinal tract since that time.

Her next hospital admission was to the Unity Hospital, Brooklyn, New York, on April 20, 1945, with chief complaints of pain in the lower back region of two weeks' duration, vaginal bleeding of one week's duration, and pruritus of the external genitals for the past fifteen years. The past history included gastrectomy in 1941 as noted above, asthma and hay fever of three years' duration, lifelong chronic bronchitis, three attacks of lobar pneumonia, hypotension, and a lipoma of the leg surgically removed in 1925.

Obstetrically, Mrs. J. P. had two miscarriages, then four normal children; all are at present living and well. Her menopause occurred at the age of 38 years.

On examination, a 65-year-old, well-developed, well-nourished white woman was seen lying comfortably in bed, complaining of "gas" pains. Her head and eyes were normal, and ears nose, and throat were negative. Neck—trachea in

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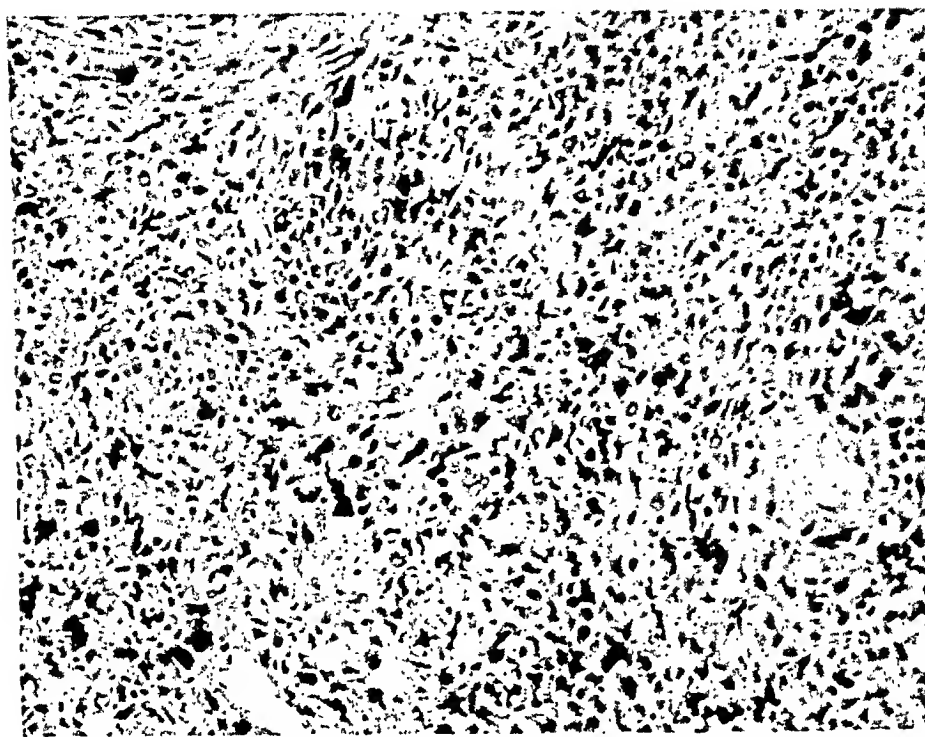


Fig. 2.—Low power. Variation in staining qualities of cells which are growing diffusely. ( $\times 180$ .)

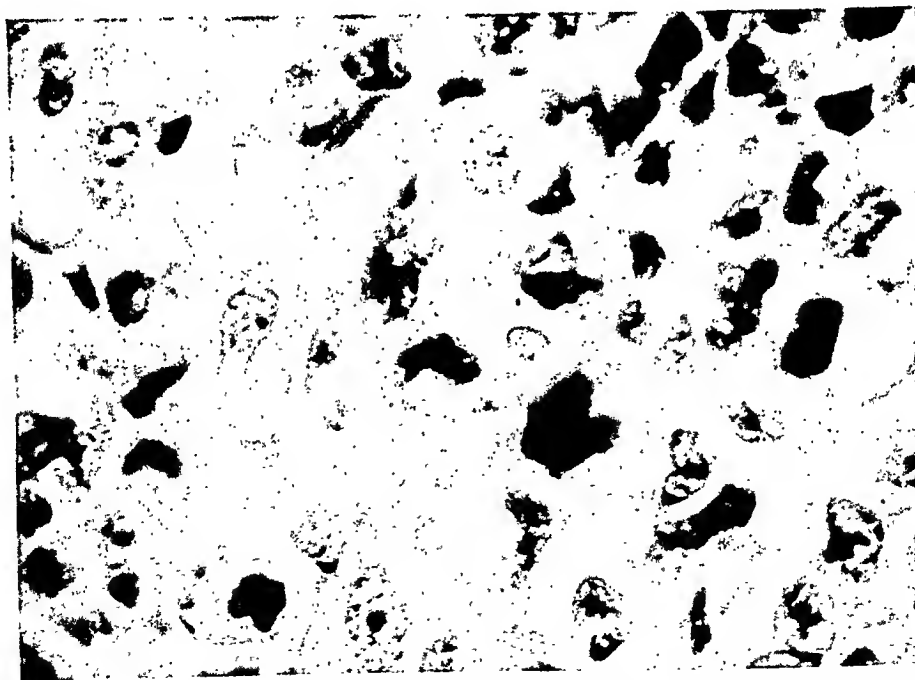


Fig. 3.—High power. The diffuse growth of cells that are unequal in size and shape with marked anaplasia and variation in staining qualities can be more plainly seen. ( $\times 750$ .)

midline, thyroid not enlarged, no palpable glands. Chest—no tumors or masses in breasts; lungs were symmetrical, slight basal râles. Heart—sounds of good quality and there were no murmurs audible. Blood pressure was 100/60. Abdomen—right upper rectus scar was well healed; soft, palpable mass two fingers above symphysis, no palpable inguinal lymphadenopathy. Extremities negative. Vaginal—multiparous introitus, sanguineous discharge from external os of cervix. Cervix normal to palpation, freely movable with no parametrial fixations. Uterus freely movable, size of six weeks' gravidity. Adnexae were



Fig. 1.—Shows extensive growth involving the cervix and fundus of the uterus. This tumor invades the thickness of the wall in various areas.

negative. An impression diagnosis of adenocarcinoma of the uterus was made and, in view of the patient's physical condition and past history, a curettage with insertion of radium was advised. This was performed under sodium pentothal anesthesia on April 21, 1945. A considerable amount of tissue resembling placenta was removed, and 50 mg. of radium was then inserted in a lead-enclosed capsule and left in the uterus for 4,800 millicurie hours; the vagina was packed with petrolatum gauze and a retention catheter placed in the urethral orifice.



## MESENTERIC LYMPHANGIOMA WITH INTESTINAL OBSTRUCTION COMPLICATING UTERINE CARCINOMA AND FIBROMYOMA

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CYSTS of the mesentery are rare surgical and very infrequent autopsy findings. Since the first reported case by Benevieni in 1507, who found a small cyst of this type at autopsy, there have been sporadic reports in the literature concerning their nature and their frequency. Dowd's frequently noted paper appeared in 1900, and for the first time the hydatid and malignant forms of mesenteric cysts and tumors were separated from the larger group of tumors which Dowd believed to be embryonic in origin. Dowd's extensive study of various types of mesenteric cysts stimulated interest in the subject. In 1927, Swartley, in reporting two cases of his own, gave an excellent review of the subject to that date with comments on diagnosis, treatment, complications, and bibliographic references. The most extensive bibliography is to be found appended to the article in 1932 by Warfield, in which he brought the subject of mesenteric cysts up to date by reviewing data on 129 case reports in the literature since 1920. Up to 1900, there had been 145 published cases, and since 1920, 129. Warfield believed that a fair estimate of the number reported in the literature to date would be between 400 and 500. Watson and McCarthy, reporting on 1,056 tumors of the blood and lymph vessels occurring between 1931 and 1939 at the Memorial Hospital, recorded only 41 lymphangiomias. None were intra-abdominal, but were located mainly on the head, neck, and extremities, with 4 per cent on the trunk. At the Mayo Clinic, Guernsey collected 15 cases of true omental cysts between 1907 and 1938. Two other cases were added to their clinic number in 1941 by Gray and Sharpe. The presentation of the latter two cases were accompanied by the comment that, although rare pathologic specimens, they were representative of a large group which demanded explorator laparotomy as the only possible method for making a definite diagnosis. Peterson reported five mesenteric and one omental cyst in 1932, all operated upon without mortality.

From the literature, the surgical pathology, and the postmortem studies on cases reported to date, it is possible to draw a fairly accurate picture of these mesenteric tumors as they are now regarded.

Lymphatic mesenteric tumors are unquestionably the *rarest tumors of the abdomen*. Of the true mesenteric tumors, the cystic are four times more frequently encountered than the solid growths. Opinion as to their origin is still divided, but the common concept is that they arise from embryonic remnants and sequestered tissues in the mesentery. In the development of the lymphatic system, it is a prevailing opinion that the lymph spaces are formed in situ by the fusion of mesenchymal spaces, and these are transformed into endothelial-lined spaces by the action of young mesenchymal cells. At first discrete, they later fuse into continuous channels. From lymphatic nests of such mesenchymal cells still retaining their embryonal character and capability for growth originate lymphatic tumors of various sizes characterized by endothelial-lined cavities containing fluid of lymphlike nature. Such tumors are usually congenital in origin, yet they rarely appear until later life. Their location varies widely, for they may be found in any site where lymphatic tissue predominates, most commonly the lips, tongue, cheek, and pharynx. They are seen somewhat more frequently in females, at all ages, and various sizes. Peculiarly enough, they

The pathologic report of the uterine curettings read as follows: "There is a marked amount of blood and necrotic tissue, but here and there are islands of atypical darkly stained cells with hyperchromatic nuclei which do not attempt to take any definite formation. The neoplastic cells themselves are very scanty in the specimen. Diagnosis—anaplastic carcinoma of the uterus (grade III—R.S.)."

Following removal of the radium, the patient bled considerably. Transfusions were given and, on April 27, 1945, a panhysterectomy was performed.

The uterus (Fig. 1) measured 10 by 5 cm. The external surface was roughened and irregular. The cervix was attached, and showed that the vaginal portion was glistening white color. The cavity of the tumor was markedly necrotic and dull gray in color, and was friable. Tubes and ovaries showed nothing of note. Diagnosis—anaplastic carcinoma of the uterus.

Fig. 2 shows a low power magnification in which the staining qualities of the cells are varied and are growing diffusely.

Fig. 3 shows more plainly the diffuse growth of cells, unequal in size and shape, with marked anaplasia.

The patient made an uneventful recovery and was discharged on May 18, 1945. At the present writing (January, 1946) there is a well-healed midline scar, no loss of weight, no lymphadenopathy, and no parametrial involvement on vaginal examination.

### Summary

1. A case of multiple primary carcinomas is presented, one an adenocarcinoma of the stomach, and the other an anaplastic carcinoma of the uterus (grade III). This occurred in an elderly female during a four-and-one-half-year period with apparent cure through surgery.

2. It is emphasized that the immunity theory for primary carcinomas is to be disregarded. On the other hand, we are to be more conscious of the appearance of new primary carcinomas in patients who have already been susceptible to one.

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The diagnosis made was probable adenocarcinoma in a fibroid uterus, or possibly a sloughing fibroid. She was immediately referred to the hospital for diagnostic studies, endometrial biopsy, and sulfonamide therapy.

*Preoperative Study.*—Admission blood count showed hemoglobin, 84 per cent; 4.41 million red blood cells; 17,200 white blood cells, 63 per cent mature polymorphonuclears, 8 per cent band, 24 per cent small mononuclears. The urine was concentrated, 1.022 specific gravity, 1 plus albumin with a few red blood cells and white blood cells per high power field. Blood sugar showed 115 mg./100 c.c.; nonprotein nitrogen, 30 mg; chlorides, 410. The blood type was "O Rh positive." Suitable donors were obtained.

From a diagnostic ennetage Sept. 8, 1944, under intravenous sodium pentothal, the pathologic report was *adenocarcinoma of the uterus*.

Her clinical condition improved on September 9 and 10, but obstructive symptoms appeared on September 11, when pathologic report of adenocarcinoma of the fundus was received. The preoperative diagnosis was (1) fibromyomatous uterus with adenocarcinoma of the fundus, and (2) partial intestinal obstruction, probably from loop of bowel adherent in the cul-de-sac or pelvis to the uterus.

*Operative Findings.*—Operation was performed Sept. 11, 1944, under spinal anesthesia, using 150 mg. of novocain. The abdomen was considerably distended. After induction of anesthesia, an abdominal mass was palpable in the umbilical region. Since adenocarcinoma of the fibroid uterus had been definitely diagnosed, a lower right paramedian incision was made. When the abdomen was opened, a large irregularly nodular mass was found in the mesentery of the small intestine. Careful inspection showed it to be a cystic and nodular intramesenteric tumor, the size of a very large grapefruit. A length of flattened small intestine was tightly draped in a ribbonlike manner over the mass and not separable from it. A number of glands were palpable in the mesentery, but it could not be determined whether these were neoplastic or inflammatory. The liver was found to be normal. The nature of the tumor was not understood at this time. Palpation of the pelvis disclosed the large uterine noted clinically, with good-sized fibroid tumors throughout. There was no indication of cancerous extension into the adnexa or broad ligaments.

In as much as mechanical occlusion of the small intestine was evidenced by hypertrophy and distention of the small bowel above the mesenteric tumor, and since it was believed at the time that this lesion represented one entirely distinct from the cancer and fibroids in the pelvis, a radical procedure was decided upon.

*Operative Procedure.*—The entire mesenteric mass was removed in toto, including about 18 inches of the overlying small intestine. The mesentery was resected to its base without encountering marked bleeding. The bowel ends were closed and inverted, a side-to-side isoperistaltic intestinal anastomosis performed; and the mesenteric defect repaired with fine chromic sutures. A complete operative change of gloves, gowns, and instruments was then made, and a radical panhysterectomy proceeded with. Except for some bleeding from the right hypogastric artery, there were no operative complications. About 5 Gm. of sulfanilamide powder was lightly scattered near the anastomosis site and in the pelvis prior to vaginal stump peritonealization, and the abdomen then closed without drainage. During the operation, 500 c.c. of blood was transfused, and subsequently 3,000 c.c. of intravenous glucose and amino acids. Pulse at the termination of the operation was 80 and her general condition considered good. Except for moderate distention lasting four days, she made a surgically uneventful convalescence.

Examinations Nov. 6, 1944, April 11, 1945, Sept. 27, 1945, and July 9, 1946, showed the abdomen to be soundly healed, the vaginal vault high, and no local

are not common in the abdomen, in spite of the extensive lymphatic system found therein. The more common of these abdominal rarities are lymphocysts of the omentum or mesentery, and these are either uni- or multilocular. Here the element of lymphangiectasis is less noted because of the tremendous accumulation of chylous fluid in a few cavities. They are seen most often in women between 30 and 50 years of age. On the other hand, the solid mesenteric lymphangioma, by scrutiny of the available data on reported lymphatic tumors, is an extremely rare type of a rare group. It is an aggregation of small lymphatic cysts and sinuses with fatty compact areas and associated edema, hemorrhage, and necrosis. In Warfield's study, one-half of the cases of mesenteric cysts were found in the small bowel, 14 of the 129 were reported in the mesentery of the jejunum, and most of these were of the single cyst type. Rarely were they noted to be solid or semi-solid structures, and only 30 were classified pathologically as lymphatic in type.

### Complications

The most common complication noted is intestinal obstruction, occurring in one-third of the reported cases, and causing a 50 per cent mortality. Peritonitis following obstruction is frequent. Torsion, fatal hemorrhage into the cyst, and rupture of the cyst into the peritoneum, are threatening complications.

The treatment of these tumors is surgical. Many are so small as to warrant no interference. The simple cysts are often enucleated without too much difficulty, but sometimes it is not possible to remove them without fatal injury to the bowel or its blood supply. Simple enucleation, when possible, carries the lowest mortality of all forms of surgical interference. In Warfield's collected series of 129 cases, enucleation with intestinal resection was performed in 22, with a mortality of over 27 per cent. Except for complications, the symptoms requiring surgical interference are largely due to the size of the growth, the interference with the passage of chyle, the mechanical burden of the tumor itself, or interference with the digestive organs by displacement and compression.

### Case Report

The patient was a female, 49 years of age, 5 feet 1 inch tall, weighing 161 pounds, with no past medical or surgical history of importance. She had two deliveries twenty-two and twenty years previously, the first instrumental, and at which she was "torn."

*Present Illness.*—For a year she had been under treatment by her family physician for a secondary anemia of obscure origin. Menstruation was regular until it stopped completely five months previously. Beginning Sept. 2, 1944, she bled heavily for five days, with accompanying abdominal cramps, gas pains, and flatulence. She was seen Sept. 7, 1944, with acute very severe lower abdominal pain, some nausea, and fever. She was referred for examination by Dr. S. Ben Asher, who diagnosed an acute abdominal condition.

Except for a mild hypertension and cardiac enlargement, there were no findings of importance other than abdominal and vaginal. The temperature was 101° F., pulse 98. The abdomen was distended, flatulent, and "potty" fat. Extreme generalized abdominal tenderness was noted, especially in the right lower abdomen. Attempts at abdominal palpation were actively resisted. Vaginal examination revealed a very lax introitus with a cystocele, rectocele, and lacerated perineum. The uterus was large and nodular, with areas of softening between numerous fibroid tumors. There was blood in the vagina, and uterine sound measurement revealed a cavity four and one-half inches deep. The adnexa were not palpable.

than 38 cm. long. The wall of the intestine is uniformly thick, has a pale serosa and a smooth mucosa. The tumor contains innumerable cystic projections with clear yellowish translucency. Other portions are solid, hard, and hemorrhagic. Cross section shows a large number of cystic cavities from which milky lymph-like fluid is discharged. The intervening stroma contains fatty yellowish tissue, quite hard, with irregular areas of hemorrhage scattered throughout. Microscopic examination shows a well-formed intestinal mucosa with the wall edematous and the serosa covered by a thin layer of fibrinous material rich in polymorphonuclear leucocytes. Red blood cells were also seen throughout the

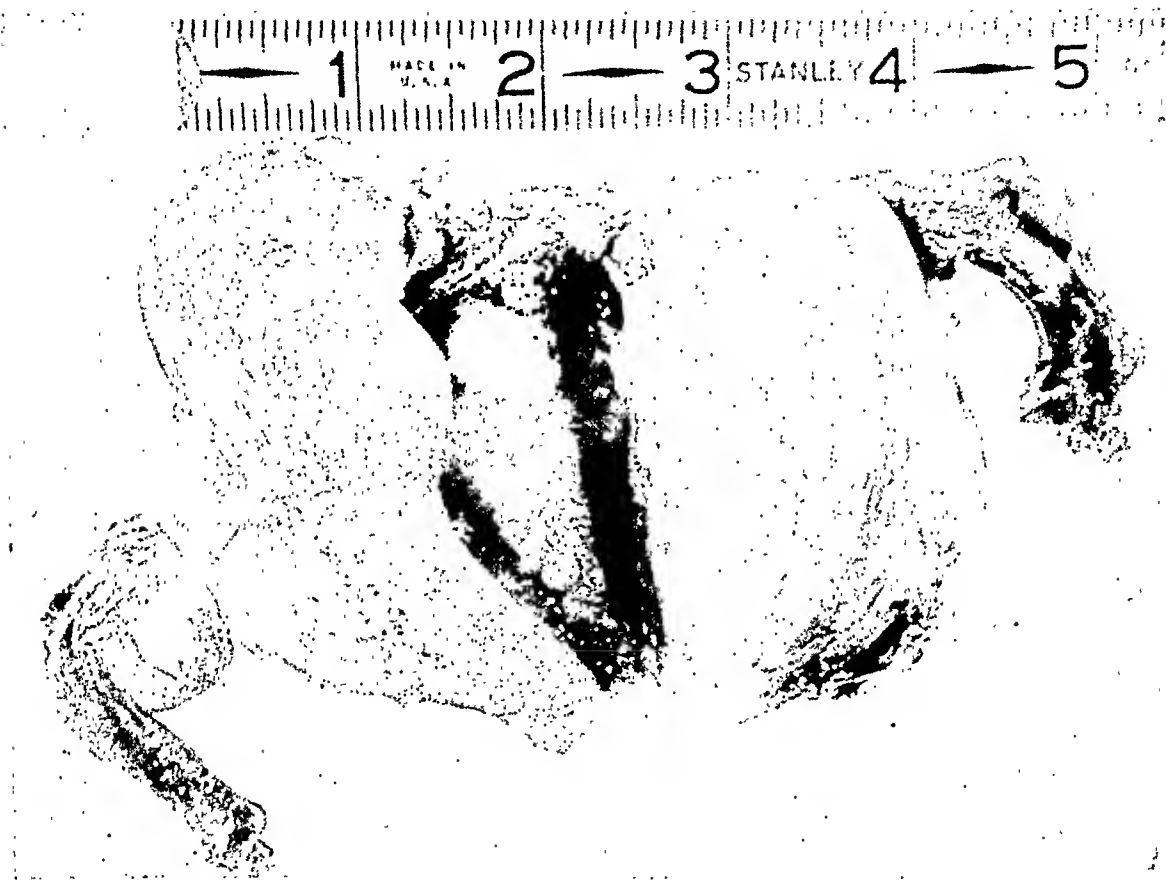


Fig. 2.—Uterus with multiple fibromyomas and fundal adenocarcinoma.

wall. Serial sections made throughout the mesenteric mass showed large cystic cavities lined by endothelial cells. The stroma showed areas of extensive necrosis with marked hemorrhages and edema and infiltration with plasma cells, lymphocytes and polymorphonuclears. The solid portion consisted mostly of polygonal fatty spaces, with marked hemorrhages and edema and necrosis throughout.

*Pathological Diagnosis.*—Early adenocarcinoma of the fundus. Multiple fibromyoma uteri with uterine sclerosis. Lymphangioma of mesentery.

### Summary

Another case of solid mesenteric lymphangioma cystica is added to the literature. In this instance the tumor caused intestinal obstruction and required intestinal resection.

evidence of any of the pre-existing lesions. Her general condition was good, with normal bowel function, and with no untoward symptoms.

*Pathologic Report.*—The specimens were examined by Dr. Nicholas M. Alter, and the following reports submitted:

There were two specimens: (1) a totally resected uterus with attached appendages. Uterus weighed 340 grams, was irregularly enlarged; the serosa was covered with adhesions and contained innumerable nodules measuring from 1 to 8 cm. in diameter. The uterine cavity was distended and contained a small hemorrhagic growth projecting from the fundus, with its base extending into the myometrium. The growth measured 2 cm. in diameter. The Fallopian

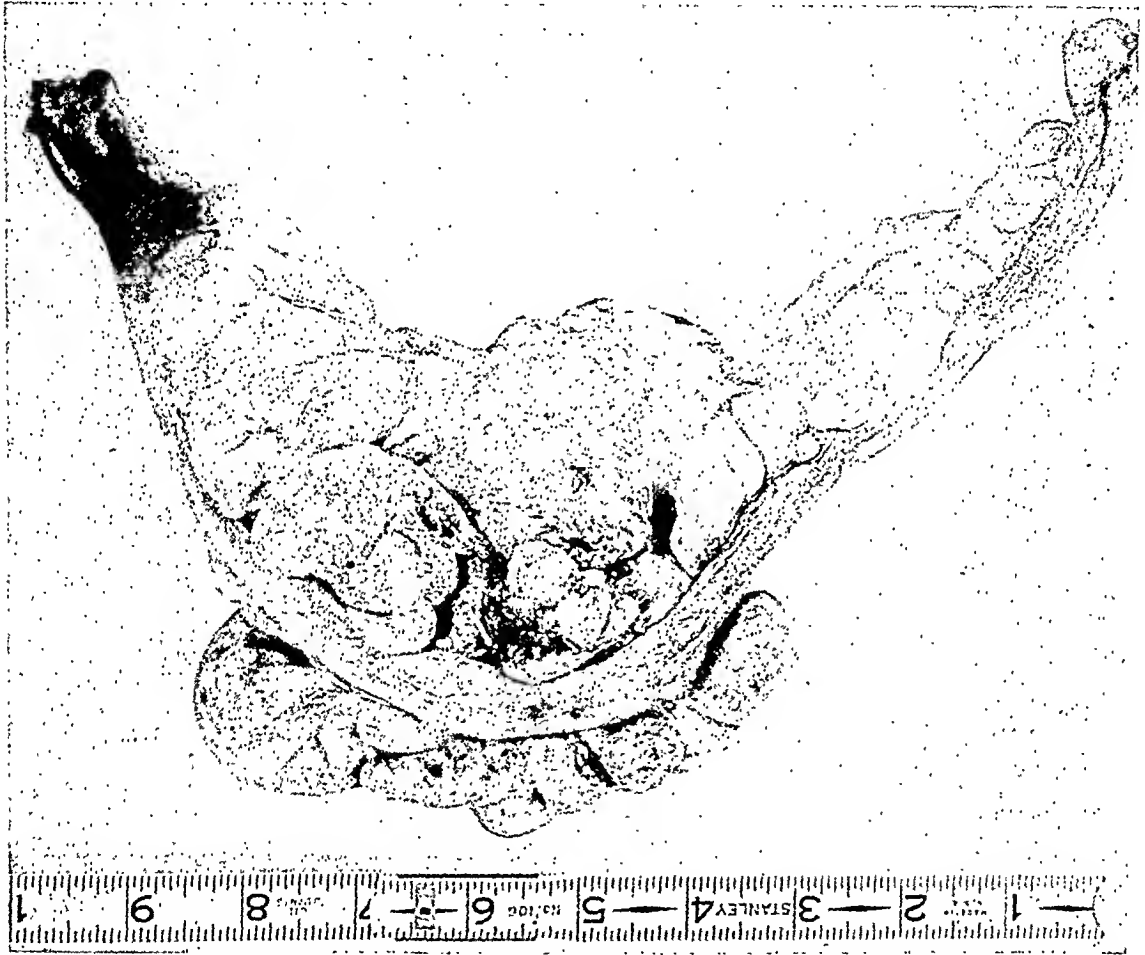


Fig. 1.—Large mesenteric lymphangioma weighing over 600 grams, with partial occlusion of the overlying ileum.

tubes were 7 cm. in length with patent fimbriated ends. The ovaries were shrunk and hard, approximately  $4\frac{1}{2}$  by  $3\frac{1}{2}$  by 2 cm., and contained small cysts. Microscopically, the uterine wall showed endometrium replaced by highly differentiated glandular growth. Glands were closely packed with anaplastic cells containing numerous mitotic figures. The glandular tissue extensively invaded the base, but not the uterine wall. The ovaries showed no ovogenesis, follicles were hyalinized, and there were some granulosa cells within the cyst wall. Nowhere in the ovaries or tubes were there evidences of growth noted in the uterus. Microscopically, the tubes were normal. (2) The second specimen was a large mesenteric mass including an overlying loop of small intestine. The mesenteric mass weighed about 800 grams and the loop of jejunum was more

## CHORIONEPITHELIOMA IN AN 18-YEAR-OLD PRIMIGRAVIDA

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**A**LTHOUGH chorionepitheliomas are a rarity, this case is unusual also because of a number of ambiguous factors. The age of 18 years is extremely young for this type of malignant tumor, although there has been a case reported in a 14-year-old girl. It is a well-established fact that chorionepithelioma occurs well over 80 per cent in multiparas.

Typical of this tumor are the marked hemorrhages so well reported in textbooks and the literature, and this case well exemplifies this fact by the enormous amount of transfused blood given the patient. Slightly in excess of 14,500 c.c. of blood was transfused, or a total of 29 pints.

A fever of uncertain origin occurred nine distinct times and, on each occasion, this followed a marked hemorrhage; this temperature varied between 104° and 105° F. It lasted from two to five days, either treated or untreated, and penicillin and sulfadiazine apparently made little difference in regard to the course of the fever. Every asset was utilized to make a diagnosis of this fever, and we finally decided it was due to necrosis of the tumor itself.

Previous to radical operation, four Aschheim-Zondek tests were made; the first, one month prior, which was reported strongly positive; the second, three weeks prior, reported weakly positive; and the final two, run simultaneously by different observers, which were reported negative. It is believed that the negative Friedman tests were due to thrombosis of the maternal vessels which prevented the escape of the trophoblast into the maternal blood stream. Six weeks and three months following surgery the Friedman tests were reported negative, indicating that perhaps a permanent cure had been achieved.

Two diagnostic curettages were performed, and neither one of them was of any value toward making the diagnosis, due to the tumor being imbedded in the myometrium, leaving the endometrial surface glistening and smooth.

The case report, in brief, follows:

Mrs. G. J. C., an 18-year-old primigravida, was seen in the Puget Sound Naval Hospital for the first time on Sept. 14, 1945; she appeared in the Out-Patient Department and was too weak to even stand erect. The following pertinent history was obtained from contacting her personal private physician.

She was married in November, 1944, and the last menstrual period was reported as November 25, 1944. On February 20, 1945, she was admitted into a private hospital, where a diagnosis of threatened abortion was made and she was sent home. On April 1, 1945, she was readmitted to this private hospital where she passed grape-like clusters, which were identified as hydatidiform mole; a curettement was performed, and the pathologist reported no evidence of malignancy in the mole. At this time she received the first of many blood transfusions.

For two months subsequent to the passage of the mole, she behaved normally and had normal menses in June and July, but in late August, 1945, she began to bleed copiously vaginally, and she was hospitalized for the third time. On entrance, a hemoglobin of 30 per cent and a red blood count of 1,870,000 cells were reported, and nothing spectacular felt on pelvic examination. She was

It complicated a hemorrhaging uterus which contained a fundal adenocarcinoma and large fibroids.

The management of the pathology is of interest. The value of radical surgery for an otherwise hopeless condition is stressed.

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transfused five times and the blood level brought nearer normal; on leaving the hospital an Aschheim-Zondek test was started. Forty-eight hours later she again began to bleed vaginally and she was rehospitalized; at this time the Aschheim-Zondek test was found to be strongly positive. This was the only definite positive reaction found at any time during the course of this disease. Hysterectomy was advised.

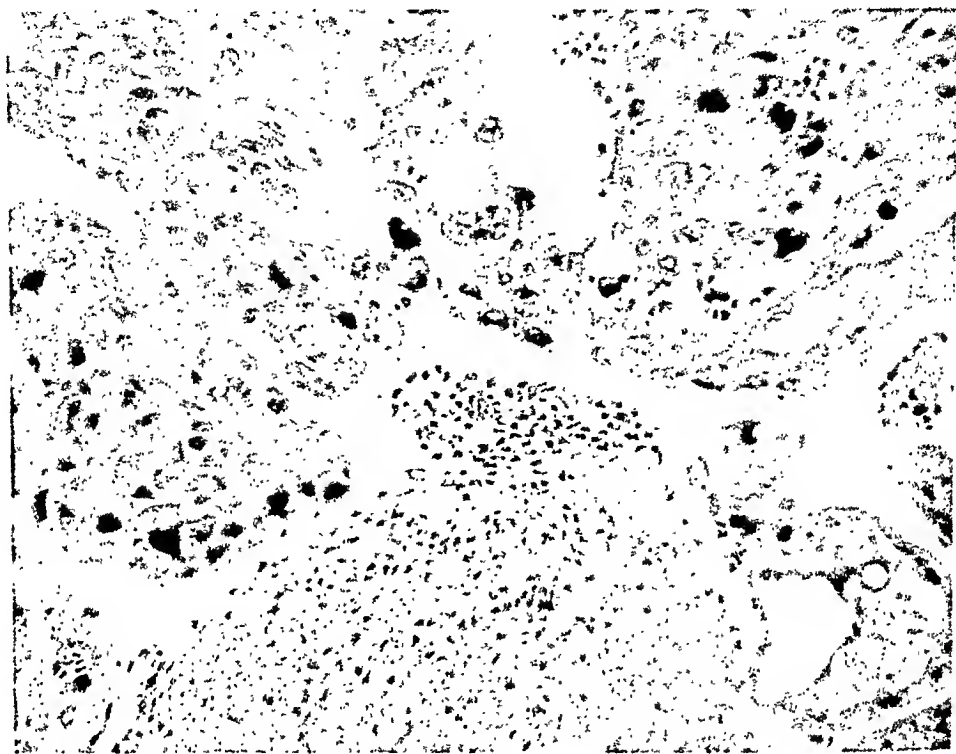


Fig. 3.—High power depicting the darkly stained syncytial cells with excellent illustrations of mitoses and amitoses. Langhans cells and lymphocytic infiltration are plentiful. ( $\times 200$ .)

On entrance, the pertinent findings were meager: the uterus was soft and the size of a six weeks' pregnancy; the patient was profoundly weak with a hemoglobin of 50 per cent and a red cell count of 3,000,000. In view of the history, a Friedman test was started immediately. The chest was x-rayed for metastases and found negative; both bleeding and coagulation times were normal, and the prothrombin time was also within normal limits; the plasma proteins were normal, and likewise the albumin-globulin ratio. While awaiting the Friedman test, she was thoroughly examined from a medical standpoint with entirely negative results. She then had a copious hemorrhage estimated at 1,500 c.c. This was replaced. The rabbit test was found to be weakly positive. Because of her age and the conflicting tests, a diagnostic curettage was performed and about 0.5 Gm. of tissue found. The pathologic report was placental tissue with no evidence of malignancy. We thought at this time she had become reimpregnated, but considered a chorionepithelioma seriously. After another week of hospitalization the pelvic examination was negative, and, as she had no vaginal bleeding, she was discharged with the advice to rest and report in another ten days for a repeat Friedman test.

A few days after leaving the hospital she had another vaginal hemorrhage; she was rehospitalized and two separate Friedman tests were started by two separately acting pathologists. One Friedman test was run with blood serum and the other with urine. Her blood level was brought to normal while awaiting

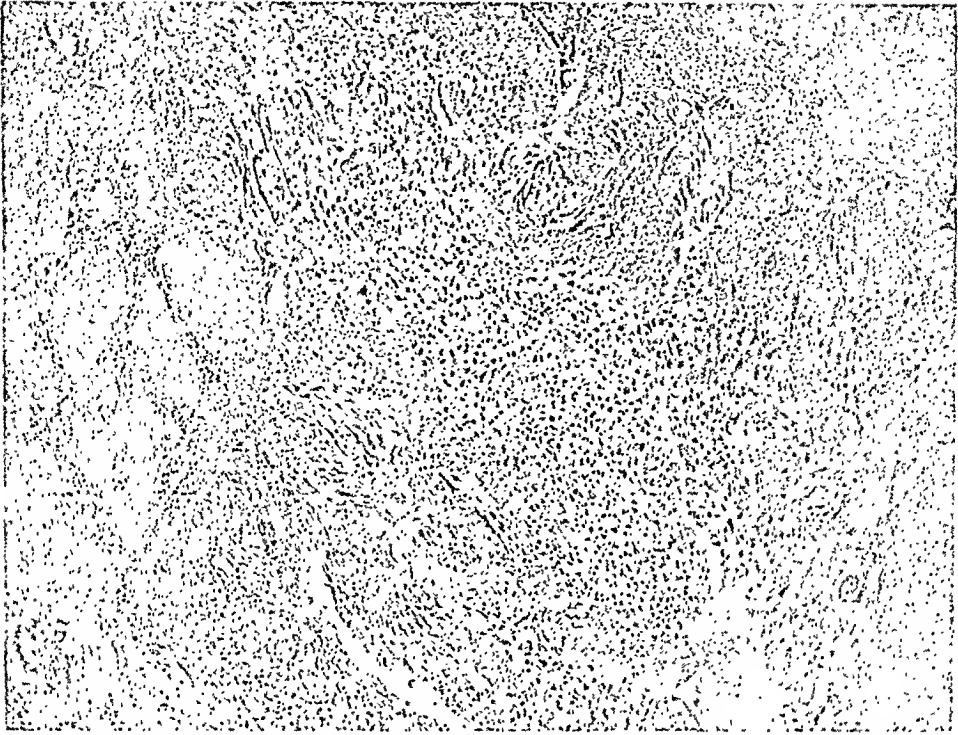


Fig. 1.—Low power revealing the invasive trophoblastic tissue in the myometrium. ( $\times 35$ .)

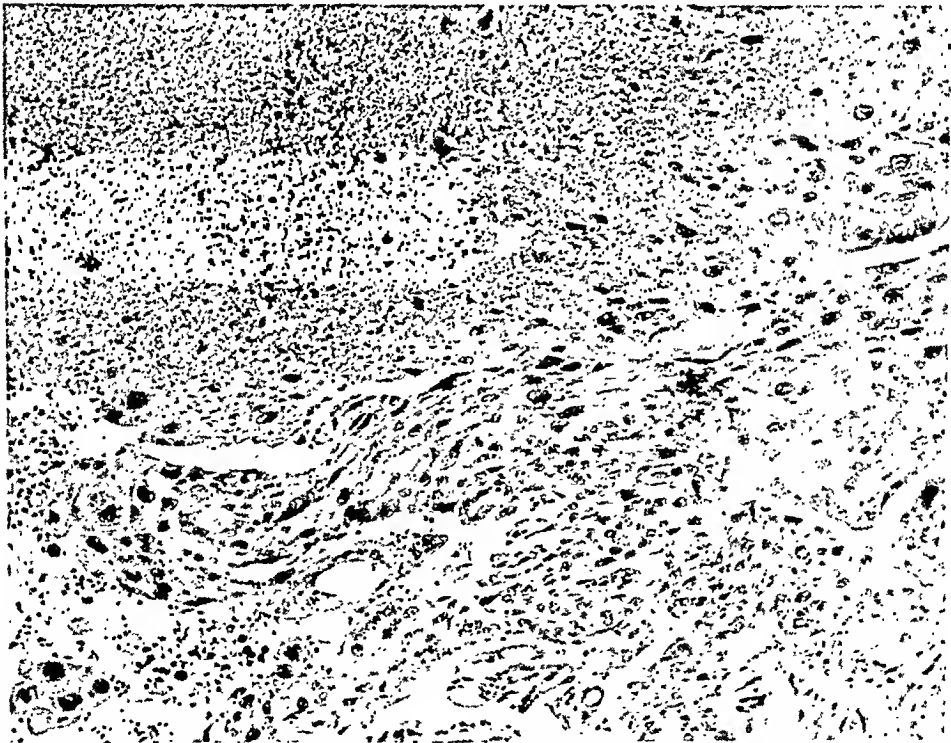


Fig. 2.—Medium high power showing round cell infiltration and syncytial island masses of sharply stained dark nuclei. ( $\times 100$ .)

## CEREBROVASCULAR COMPLICATIONS OF PREGNANCY

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THE cerebrovascular complications of pregnancy deserve attention for the following reasons: (1) gross brain hemorrhage is found in 15 to 20 per cent of autopsies on eclamptic patients, which is in contrast with the infrequency of clinical diagnosis; (2) appreciable brain hemorrhage imposes a mortality rate in excess of 50 per cent, and ranks as the second most common cause of death in eclampsia; (3) areas of softening or encephalomalacia are relatively frequent, may produce death in the absence of hemorrhage, and are commonly unrecognized; (4) finally, there is evidence to indicate that patients with sufficient vascular damage to produce fatal hemorrhage or softening should not always be diagnosed as "eclampsia," even in the presence of hypertension, albuminuria, edema, and convulsions. These points are illustrated in the following three reports.

CASE 1.—Mrs. C. G., Hospital No. W26329, a 36-year-old gravida ix, para vi, entered the hospital in labor. She had received no prenatal care. She had "fits" with her first pregnancy, but there was no history of hypertension or renal disease. The blood pressure was 195/92 on admission, and there was moderate ankle edema. A voided urinary specimen contained a trace of albumin, a few red blood cells, and no casts. Her temperature was 99.4° F. The obstetric course in the hospital was characterized by uterine inertia. In the ensuing twenty-one hours, the patient received intravenously 2,000 c.c. of 5 per cent dextrose in water and sedation with morphine and scopolamine. Later in the day, urine obtained by catheterization contained a trace of albumin and was loaded with hemolyzed red blood cells, but no casts. The blood pressure remained elevated but at a lower level than the reading on admission. Twenty-one hours after admission the temperature rose to 102° F. and, therefore, the patient was given 1,000 c.c. of 5 per cent dextrose in water by hypodermoclysis. Three hours later the temperature was 104.4° F. Pulmonary edema developed and rapid digitalization was instituted. Two hours thereafter, the patient became comatose, the temperature was 107° F. and subsequently rose to 110° F. The patient became markedly cyanotic and dyspneic and expired undelivered, thirty-one hours and twenty minutes after admission.

Postmortem examination revealed generalized slight arteriosclerosis, medial necrosis of the thoracic aorta, perivascular hemorrhage throughout the brain, and an area two centimeters in diameter of encephalomalacia in the hypothalamus.

CASE 2.—Mrs. B. J., Hospital No. W27509, a 20-year-old primigravida, entered the hospital in labor. She had received no prenatal care. There was no history of hypertensive or renal disease. On admission, the blood pressure was 220/156, and there was marked edema of the legs and ankles. Repeated urinalyses of specimens obtained by catheterization revealed large amounts of albumin, occasional red blood cells, and granular casts. Blood chemistry determination the day of delivery showed slight elevation (5.6) of uric acid levels, normal creatinin, and reduced serum albumin levels (3.2), with reversed albu-

the results of the biologic tests. Both were reported negative. A curettement revealed only a small fibrin blood clot. She was then subjected to a major operation.

Notwithstanding her age, two negative diagnostic curettements, and two negative Friedman tests, we felt rather positive of the diagnosis of chorionepithelioma. After appropriate transfusions, an abdominal hysterectomy was performed. This was done without incident, and there was no evidence of metastases anywhere in the pelvic or abdominal cavity. She made an uneventful recovery and was discharged on the fourteenth postoperative day. Six weeks following surgery a pelvic examination was negative, the chest plate negative, the blood count normal, and the Friedman test reported negative. Three months post-operatively another Friedman test was negative, and the patient was apparently well on the road toward permanent recovery; but she was advised to have biologic tests from time to time in the future.

The pathologic report was as follows:

The posterior and superior aspects of the vault of the uterus contained a coarsely granular, dark red mass which measured 5.5 cm. in diameter. Cut surface of this mass revealed the myometrium, which measured 1.8 cm. thick, to be invaded by semi-firm, dark red tissue for varying distances up to 1.6 cm. The tumor mass seemed confined to the myometrium, as the endometrium was pinkish red, smooth, thin, and glistening. Microscopic examination revealed the mass to consist of edematous connective tissue which was infiltrated with round cells, trophoblasts, and red cells which formed island cords. The myometrium was edematous, and the cells hypertrophied, and the intermuscular tissue infiltrated by trophoblasts. Both syncytial and Langhans cells were readily identified with the former, showing numerous mitoses and amitoses in the darkly stained nuclei. *Diagnosis:* chorionepithelioma with progestational hypertrophy of the uterus.

### Conclusions

The Friedman test is valuable but not conclusive in the diagnosis of chorionepithelioma. The diagnosis must still be based on the clinical history and findings on physical examination. It is recommended that Friedman tests always be run and preferably quantitative tests after every case of hydatidiform mole, but to remember always that a chorionepithelioma might still be present with a negative test.

False Friedman tests in this case were not due to the rabbits which were carefully checked and not due to the individual performing the actual test, but more likely due to the blockage of the escape of the trophoblast into the maternal blood stream.

Curettement can be useless in the diagnosis, as proved by this case and also by two other cases reported in the literature; these negative diagnostic curettages were all due to the tumor being interstitial and not encroaching on the endometrium.

Fever and rigors following hemorrhage in the presence of a chorionepithelioma are most likely due to necrosis of the tumor and are unaided by penicillin and chemotherapy.

she was treated for "stroke" and high blood pressure. On admission the blood pressure was 246/130. The reflexes were hyperactive but equal, the right eye looked down and outward. There was no edema. Urine obtained by catheterization contained large amounts of albumin and occasional red blood cells. The spinal fluid was clear with a pressure of 220 mm. of water and contained 100 mg. per cent of protein. Subsequent examination showed progressive rise in pressure with appearance of gross blood. The reflexes gradually disappeared, the temperature rose terminally to 109° F., and the patient expired twenty-eight hours after admission.

Postmortem examination revealed generalized arteriosclerosis, nephrosclerosis, and cardiac hypertrophy. There was an area of recent hemorrhage in the midbrain just above the pons, at the region of the cerebral peduncles and corpora quadrigemina. The hemorrhagic area was 3 cm. in diameter with surrounding encephalomalacia of indefinite extent. It should be noted that this patient, whose findings and course so closely resembled those of the other two, was not pregnant.

### Comment

Accidents of such gravity demand a consideration of the factors involved in their production. With vessel disruption sufficient to produce gross hemorrhage, one would logically expect to find a pre-existing lesion of the vessel wall. Since normal vessels can withstand unbelievably high pressure over a long period of time, something more than pressure itself is necessary, as Dieckmann<sup>1</sup> has pointed out. Types of pre-existing organic lesions include the chronic vascular changes of essential hypertension, the vascular lesions of syphilis, or congenital aneurysm.<sup>2</sup> It is at once apparent that these are not the lesions commonly associated with the so-called "true toxemias of pregnancy," preeclampsia and eclampsia, in which reversible vasospasm is generally the predominant or only vascular lesion. Nor are these chronic vascular changes in any way peculiar to pregnancy, as illustrated by the third case report.

However, the second patient described presented none of the above vascular lesions. Some other explanation of the fetal hemorrhage must be sought. Spasm of a cerebral end artery may produce distal softening or encephalomalacia, in a manner similar to the production of an infarct elsewhere. Distal to the point of spasm, the vessel itself may undergo softening with subsequent disruption and hemorrhage. This concept that temporary vasospasm may of itself produce permanent vascular damage takes us into the twilight zone between the reversible spastic vascular lesion of "true toxemia" and the irreversible sclerotic lesion of hypertensive vascular disease.

At any rate, three facts pertaining to encephalomalacia are worthy of note:

First, encephalomalacia of sufficient extent or location may produce fatality just as surely as hemorrhage of equivalent area. This is shown on the first patient where a strategically located area of softening only two centimeters in diameter was the major cause of death.

Second, the lesion may result from spasm of a previously normal cerebral vessel. This is shown in the second patient who lacked microscopic evidence of arteriolar disease.

Third, the syndrome of spasm and resultant encephalomalacia with or without hemorrhage is probably the only satisfactory explanation for cerebro-

min-globulin ratio. Four hours and thirty-three minutes after admission she was delivered spontaneously of a 3,041-gram female child. The blood pressure fell during labor and for twelve hours thereafter, and then began to rise. Seventeen hours post partum it was 220/150. Nineteen hours after delivery, the patient suffered a two-minute convulsion, followed by coma and marked Cheyne-Stokes respirations. The blood pressure at this time was 240/90, and the temperature was 105° F. In the next twelve hours the blood pressure fell to 160-180 systolic and 80-90 diastolic, and the temperature varied between 101° and 102° F. During this time, however, evidence of left hemiplegia and right oculomotor paralysis developed. The spinal fluid was under a pressure of 152 mm. of water and contained 188 red blood cells per cubic millimeter and 224 mg. per cent of protein. Between thirty and eighty hours post partum the patient seemed to improve slightly. Then the blood pressure rose gradually to former levels and the temperature rose abruptly to 107.6° F. The patient became comatose and expired ninety-two hours post partum.

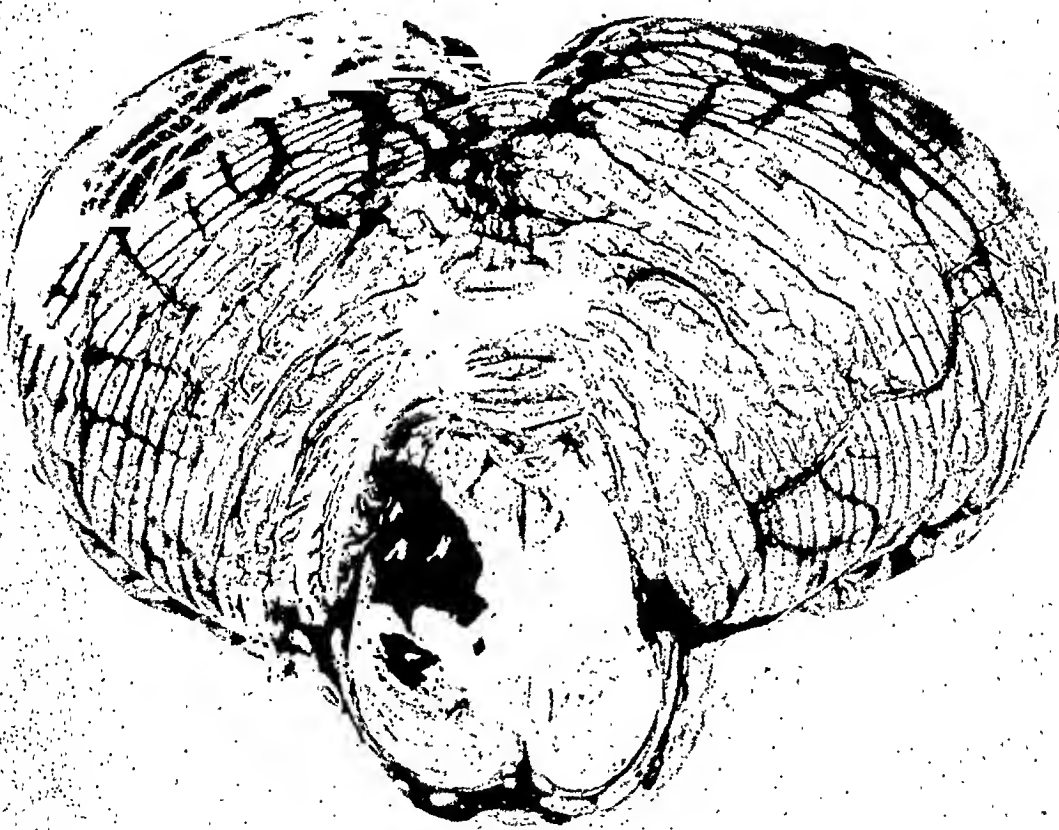


Fig. 1.—Note area of hemorrhage and encephalomalacia in the right midbrain. This section is at the level of the red nucleus.

Postmortem examination revealed a large area of hemorrhage and encephalomalacia in the right midbrain. This area was at the level of the red nucleus lying just anterior to the cerebral aqueduct, and extending to the lower portion of the pons beneath the floor of the fourth ventricle. (See Fig. 1.) There was very little microscopic evidence of chronic arteriolar or renal disease.

CASE 3.—Mrs. J. K., Hospital No. 7131, a 39-year-old gravida i, para i, entered the hospital in a comatose state. Her relatives explained that she complained of pain in the left arm before she fell to the floor. Two years before

## BILATERAL SIMULTANEOUS TUBAL PREGNANCY

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*(From the Migratory Labor Hospital)*

**S**IMULTANEOUS pregnancy in both tubes is the rarest form of double ovum twin pregnancy. A total of 84 authentic cases has been reported. Fishback<sup>1</sup> reviewed 76 cases in 1939, including one of his own, and subsequent reports have been made by Lee and Stone,<sup>2</sup> Torpin,<sup>3</sup> Behney and Hanes,<sup>4</sup> Cox and Steinberg,<sup>5</sup> Chisholm and Lesslie,<sup>6</sup> Mitchell and Kurzrok,<sup>7</sup> and Otero.<sup>8</sup> The latter's report, like that of McIlrath,<sup>9</sup> does not include a report of the microscopic pathology, but does include a gross description of the specimen and a photograph of the two fetuses.

Even less common forms of tubal gestation have been reported. Fishback<sup>1</sup> described a case with two separate pregnancies in the right tube, and one in the left, and referred to two previous similar reports. Chisholm and Lesslie<sup>6</sup> refer to a case of quintuplets found in one tubal gestation sac by Tremb of Amsterdam.

The growing list of authentic cases of bilateral simultaneous tubal pregnancy serves to emphasize the necessity of exploring both adnexal regions carefully at the time of operation. Most men agree that the treatment of choice is partial bilateral salpingectomy with preservation of one or both ovaries and the uterus.<sup>9</sup> Hysterectomy has been recommended,<sup>10</sup> but is hazardous when gross hemorrhage of any extent has occurred preoperatively. It should be considered, however, when no bleeding has occurred preoperatively in a patient near the menopause.

### Case Report

E. S., a married Negro woman, 33 years of age, was admitted to the Migratory Labor Hospital, Belle Glade, Florida, on Aug. 10, 1945. One hour before admission she had been seized with a sudden severe pain in the left lower abdomen, following which she felt weak and fainted.

Questioning revealed a history of six previous normal full-term deliveries, and one abortion at two months. There was no history of pelvic inflammatory disease, and her blood Kahn had been repeatedly negative. Her menses had been regular in March, April, and May, but in June and July the menses were scanty and lasted only two to three days. She had noticed occasional "spotting" throughout the last two months, and for the past two weeks had had intermittent cramping lower abdominal pain.

Examination revealed an acutely ill, anxious, Negro woman, with an obvious pallor, and complaining of abdominal pain. The temperature was 97.2° F.; the pulse rate, 90; respiratory rate, 22; and the blood pressure, 105/70. The abdomen was distended, and there was marked generalized tenderness, with rigidity of both lower quadrants. Exquisite tenderness made the pelvic examination difficult. The cervix was soft and patulous, and the uterus was slightly enlarged and soft. There was a tender, cystic mass in the left fornix. No mass was discerned in the right fornix.

The patient was transfused with whole blood at once, and a laparotomy was performed. At operation the abdomen was found to be filled with fresh blood and numerous older clots. A dark cystic mass (Fig. 1B), obviously

vaseular accident in the pregnant woman without hypertensive vaseular disease, syphilis, or congenital aneurysm.

It should be emphasized that failure to perform adequate neurologic examination in the toxemic patient will usually preclude understanding of the true nature of the lesion unless the patient comes to postmortem examination. From the clinical standpoint, such failure will necessarily mean incorrect diagnosis, erroneous classification, insufficient grasp of the gravity of the situation, and improper treatment.

Finally, it should be borne in mind that certain intracranial hemorrhages are amenable to surgical approach, and early diagnosis with adequate treatment has actually been lifesaving.<sup>3</sup>

### Summary

1. Cerebrovascular complications are frequently associated with toxemia of pregnancy, greatly increase the mortality rate, and often pass unrecognized.
2. These complications may manifest themselves as hemorrhage or encephalomalacia, usually depend on some pre-existing vascular lesion not peculiar to pregnancy, and therefore are not to be classified among the true toxemias.
3. In the absence of such chronic vascular disease, it is suggested that temporary vasospasm may result in distal softening with or without hemorrhage.
4. Careful neurologic examination of the pregnant hypertensive patient is mandatory if these complications are to be discovered. This is an obvious prerequisite to the institution of adequate treatment, which may improve the generally unfavorable prognosis.

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ously contained blood, but no perforation or bleeding was found. This mass was removed by partial salpingectomy. No definite corpus luteum was seen on either ovary. The free blood was sponged from the abdomen before closure. The postoperative course was uneventful.

Grossly the specimens consisted of a portion of the respective tubes, distended with old clotted blood. No fetal parts or membranes were found grossly in either specimen. Since the masses were formed entirely from the blood clots, no inference as to the relative age of the two pregnancies can be assumed from the discrepancy in their size.

Microscopic study revealed chorionic villi in both specimens. Villi from the right tube (Fig. 2A) were somewhat less autolysed than those from the left tube (Fig. 2B).

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containing clotted blood, distended the distal third of the left tube, and protruded somewhat through the fimbriated end. The mass was firmly adherent to the left ovary, and there was free bleeding from a raw area on the pos-

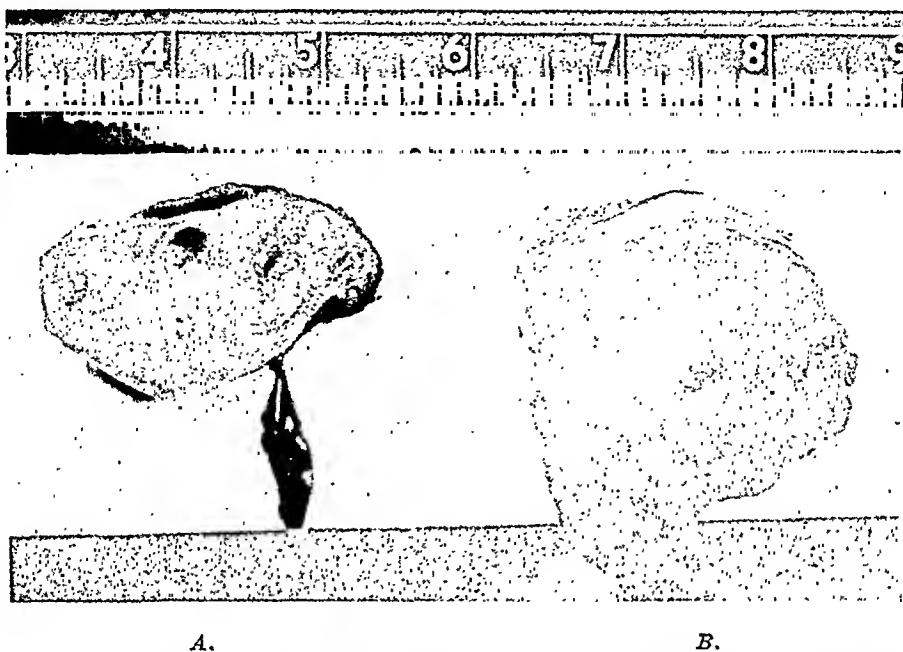


Fig. 1.—A, shows the middle third of the right tube with its unruptured pregnancy. The attached blood clot is from the mesentery. B, shows the distal one-half of the left tube and its ruptured tubal pregnancy.

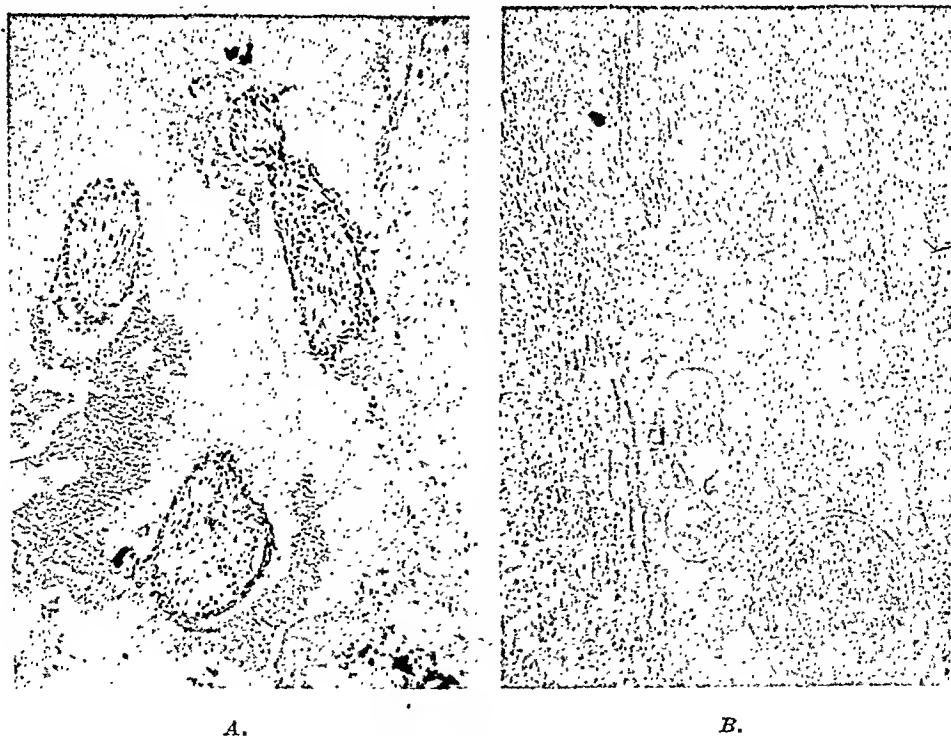


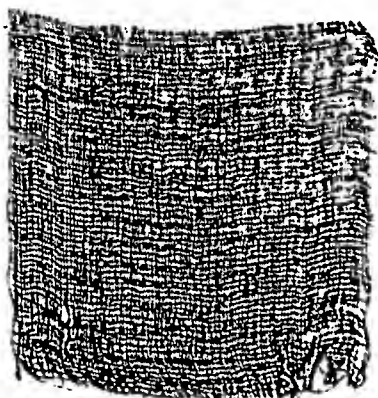
Fig. 2.—Chorionic villi from the right tube are shown in A, and from the left tube in B.

terior surface. The mass was removed along with the distal one-half of the tube and the ovary. Exploration of the right tube revealed a similar smaller mass (Fig. 1A) distending the middle one-third of the tube. This mass also obvi-

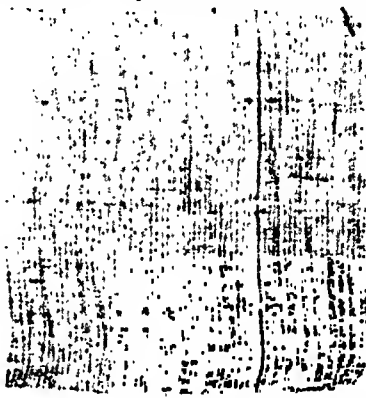
The implanted material went slowly into solution, being excreted from the blood stream, mainly by the kidneys. In addition, some of the material was carried away by phagocytes, not as particulate matter, but in solution, causing intense basophilic staining of the cytoplasm. No evidence of any significant kidney damage due to the passage of the material has been noted. In serous and synovial cavities, cysts may form about the gauze; these are thin-walled, without evidence of inflammation, and contain clear fluid. Frantz believes that these formations eventually disappear. This material will be referred to as absorbable gauze in the balance of this report.

## GAUZE

Before and After Oxidation on Stretchers.  
(Samples the same size originally by thread count)



UNTREATED



OXIDIZED

Fig. 1.

With the experimental proof that oxidized gauze was not irritating to tissues, was readily absorbed, and possessed remarkable hemostatic qualities, the material became available for clinical use in the gynecologic operation rooms of the Sloane Hospital for Women in January, 1945. Since this date it has been utilized in 30 cases to control hemorrhage from various sites. These cases may be classified into several groups, and illustrate the rather wide field in which this new hemostatic agent may be conveniently and usefully applied.

### Abdominal Operations (Fifteen Cases)

1. Absorbable gauze was utilized on nine occasions to control the oozing from raw surfaces of the pelvic peritoneum after the liberation and removal of adherent inflammatory, endometriotic, or neoplastic adnexal masses. One or more squares of gauze were placed against the oozing area and held in place for a few minutes. In six cases the oozing promptly ceased, following which the abdomen was closed. In two cases bleeding recurred following the release of pressure. In order to maintain pressure, plain gauze packing was placed on top of the absorbable gauze and led out through the lower angle of the wound. On its removal in twenty-four hours, it proved to be only slightly stained with blood, and little discharge was present on the abdominal dressing. In the remaining case drainage was necessary because of an accidental injury to the sigmoid.

# ABSORBABLE (OXIDIZED) GAUZE AS A HEMOSTATIC AGENT IN GYNECOLOGIC SURGERY\*

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**D**URING recent years there has been a reawakened interest in the development of hemostatic agents and in their application to the various fields of surgery. Fibrin foam,<sup>1</sup> gelatin sponge,<sup>2</sup> and oxidized cellulose<sup>3</sup> have been the principal materials subjected to investigation. The first two materials are used in conjunction with thrombin solution to produce their hemostatic effect. Oxidized cellulose, while it has been used with thrombin solution,<sup>4, 5</sup> appears to be a hemostatic agent in its own right. Its capacity for producing hemostasis without the addition of thrombin makes its application simpler than in the case of the gelatin and fibrin preparations.

Oxidized cellulose was first prepared by Kenyon and his collaborators (U. S. Patent 2,232,990).<sup>6, 7</sup> They found that cellulose in any form, paper, cotton, or gauze, could be oxidized by nitrogen dioxide. Due to the extensive carboxyl formation, the original qualities of the material were altered. Considerable shrinkage occurred, some of the tensile strength was lost, and the color was often not as white as the original, frequently being somewhat yellow. Shrinkage has been minimized by the oxidation of gauze on stretchers (Fig. 1). Its most important quality from a surgical point of view lies in its slow solubility in a 0.15 molar solution of sodium bicarbonate, the pH of which approximates that of the blood. Its most striking disadvantage lies in the fact that it disintegrates in the autoclave and only withstands boiling for three minutes. It has, therefore, been subjected to formaldehyde sterilization.†

Frantz et al<sup>3, 8-10</sup> have studied the response of animal tissues to all these forms of oxidized cellulose. As additional qualities became evident during the course of her experiments, she became chiefly interested in the oxidized gauze. She performed implants of this material in a large variety of animal tissues, such as connective tissue, bone, and serous and synovial membranes, and in the parenchymatous organs, such as the brain, thyroid, liver, kidney, and spleen. She found this material relatively nonirritating, producing little reaction, and eventually completely absorbable. The time of absorption was dependent on the amount of material introduced, the extent of the operative trauma, and the quantity of blood present in the gauze. She noted that oxidized cellulose appeared to have a specific affinity for hemoglobin, absorbing it from solution and forming a chemical combination turning the gauze brown. When placed in contact with whole blood, it rapidly formed a brownish-black gelatinous mass; its bulk increased during this process. Its behavior when saturated with whole blood accounts for its hemostatic qualities. In her experimental work Frantz discovered that the hemorrhage from freely bleeding lacerations of the kidney, liver, and spleen was quickly controlled when the wounds were packed with oxidized gauze.

\*Presented at a meeting of the New York Obstetrical Society, March 12, 1946.

†Both gauze and cotton are now prepared in the research laboratories of the Eastman Kodak Company and are sterilized and packaged by Parke Davis and Company, and by Johnson and Johnson.

2. Secondary hemorrhage from the vagina: (a) Three cases were encountered in which profuse secondary hemorrhage occurred on the fifteenth, eighth, and eighth days following the performance of vaginal plastic operations. All of them were put under anesthesia and, on examination with a bivalve speculum, were found to have areas of disruption in the vault of the vagina. One or more squares of absorbable gauze were placed against the areas and held in position with plain packing. This promptly controlled the bleeding. The plain packing was removed in twenty-four hours. In no instance did any bleeding recur. The absorbable gauze was discharged as brownish particles over the next seven to ten days.

*Comment.*—Previous experience with this type of case has shown that the bleeding is not often controlled by ordinary gauze packing and that ligation and resuture have been necessary. The exposure necessary for the latter procedure has often been detrimental to the recent plastic repair. In all three of these cases, on the other hand, bleeding was easily controlled without the production of any additional disruption. Observation of these patients later on has shown no impairment of the eventual results of their operation.

(b) In three patients profuse and violent hemorrhage occurred on the fourteenth, eleventh, and ninth days after a complete abdominal hysterectomy. Examination under anesthesia with a bivalve speculum disclosed that the source was a disrupted vaginal vault. One or more squares of gauze were placed against these areas and held in position with ordinary vaginal packing. The hemorrhage was promptly controlled. The subsequent treatment and course was similar to that of cases suffering from secondary hemorrhage following vaginal plastic operations.

Of the remaining patients one had a secondary hemorrhage two days after a cauterization of the cervix. Plain gauze packing failed to control this, but it promptly stopped when absorbable gauze was placed against the area, plain gauze being used to hold it in place. The other had a secondary hemorrhage from a biopsy wound of the cervix on the seventh postoperative day. The same measures served to control this bleeding.

### Summary

Experience with absorbable gauze during the past ten months has shown that it was frequently useful in controlling bleeding during abdominal gynecologic operations. It should in no sense replace the careful control of hemorrhage by clamp and ligature. However, when bleeding was difficult to control by such methods, either because of its oozing character or because the source of hemorrhage was not readily accessible, absorbable gauze was found to have a definite place as a hemostatic agent. Its application to the area of bleeding followed by momentary digital pressure was successful in most instances. When, in a few cases, hemorrhage recurred following the removal of digital pressure, satisfactory results were attained by superimposing ordinary packing. The latter material was removed in twenty-four hours with evidence of a minimal amount of bleeding in the interim, and no recurrence of bleeding following its removal. The early complete removal of plain packing without fear of provoking fresh hemorrhage was a great advantage. No reaction could be traced to the leaving of varying amounts of oxidized gauze within the abdominal or pelvic cavities. A few unusual applications of it during abdominal operations have been mentioned. Undoubtedly others will occur as experience in the application of this material grows.

2. Absorbable gauze was used to control retroperitoneal bleeding on four occasions. In two cases the bleeding arose following the enucleation of intraligamentous fibroids. In one of these patients the oozing area in the bed of the tumor was quickly controlled by the application of gauze and momentary pressure. In the other, bleeding recurred when pressure was released, necessitating the application of steady pressure with plain gauze packing. On the removal of this packing in forty-eight hours, little drainage was found on the abdominal dressing, and the packing itself was only lightly stained with blood. In another case bleeding deep in the bed of an intraligamentous cyst was quickly controlled by the application of gauze and momentary pressure. In the remaining patient profuse bleeding encountered during an attempted resection of the presacral nerve was controlled in the same way.

3. During a laparotomy for secondary abdominal pregnancy profuse bleeding was encountered when the margin of the placental attachment was accidentally separated. This was controlled by the application of gauze squares and momentary pressure.

4. Following the completion of a myomectomy, oozing continued from the closed incision and from suture holes. This stopped immediately following the application of gauze and pressure.

*Comment.*—In no instance was there any evidence of recurrence of hemorrhage. The postoperative course of these patients seemed in no way influenced by the varying amounts of absorbable gauze left within the abdomen either intraperitoneally or retroperitoneally.

Two deaths occurred in this group, neither of which could be attributed in any way to the use of absorbable gauze. One of these patients died of a severe pelvic infection following an injury to the sigmoid; the other, a woman 63 years of age, died of shock and cardiac failure after the enucleation of a huge retroperitoneal fibroid.

### Vaginal Operations (Fifteen Cases)

1. Bleeding occurring at time of or closely related to the operation: absorbable gauze was utilized to control bleeding or oozing on seven occasions under these circumstances. On four occasions oozing was noted from closed incisions after the completion of a vaginal plastic or amputation of the cervix. In three patients plain gauze packing was placed on top of the absorbable gauze for its pressure effect. While bleeding ceased in two instances, of the others one developed a vaginal hematoma, while the second continued to bleed in spite of packing. Her hemorrhage was controlled finally by a complete hysterectomy.

*Comment.*—Although both the latter cases could be regarded as failures, it seems obvious that the hemorrhage was not controlled because the gauze was not placed, under pressure, in immediate contact with the bleeding vessel. They may therefore be regarded as faulty applications of this new material. Under such circumstances, absorbable gauze should be no more effective in controlling bleeding than plain packing.

In another plastic operation, profuse bleeding occurred during the dissection of the prevesical fascia. Absorbable gauze was packed against the bleeding area, immediately controlling the ooze. The fascia was united in the midline, and the vaginal wall was closed over it. No abnormality occurred during the postoperative course, and healing appeared to be perfect on discharge. In contrast with the group of cases just considered, this would appear to be the proper method to employ with this material in vaginal operations.

In the remaining patients absorbable gauze with superimposed vaginal packing was used to control bleeding from the crater of a carcinomatous cervix, and from a biopsy wound which proved difficult to suture. In both instances hemorrhage was promptly controlled.

## RUPTURE OF THE POSTERIOR VAGINA DURING NORMAL COITUS

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(From the Department of Gynecology, Norfolk General Hospital)

THE purpose of this paper is to report an unusual vaginal injury produced during normal coitus.

Mrs. M. G. was first seen in the emergency room of the Norfolk General Hospital about 3:00 A.M., Sept. 26, 1945. The history and hospital course are as follows: The patient came to Norfolk from a near-by state on the morning of September 25 to be with her husband, who was in the Navy. She had not been with her husband for six months. The couple had been married two years. The patient had been pregnant once, and had been delivered at term of a 7-pound baby, eight months before. They met in a hotel late in the afternoon, had intercourse, and went out to dinner. They returned to the hotel room and again had intercourse. There was no pain; in fact, nothing unusual was experienced by either husband or wife. Ten minutes after intercourse, she noticed a dull ache in her lower abdomen followed by excessive vaginal hemorrhage. The bleeding continued moderately for several hours with passage of clots; it did not stop; and when she became faint, she was taken to the Norfolk General Hospital. A vaginal examination showed the vagina full of clots; laceration of the right posterior wall was felt and seen. The clots were expressed and the vagina packed. The patient was in mild shock when she was admitted to the hospital. A blood examination showed: hemoglobin 7.8 Gm., 46 per cent; red blood cells, 2,500,000; white blood cells, 12,600. She was given a 500-c.c. citrated blood transfusion and taken to the operating room.

*Operation.*—The vaginal packing was removed. Examination showed a normal multiparous introitus, slightly relaxed vaginal vault, the uterine horns low, of normal size, and in a mid-position, the cervix showed a small healed bilateral laceration. To the right of the cervix was a clot-filled laceration extending through the vaginal wall. The laceration was 2 inches in length, extending from before backward and located in the right fornix. The laceration had penetrated the entire thickness of the vaginal wall, severed a small branch of the uterine artery near the cervix, and had exposed the loose areolar tissue between the vaginal wall and the cul-de-sac peritoneum. The peritoneal cavity had not been penetrated. The entire lacerated area was cleared of clots, and the spurting artery near the cervix was suture ligated with No. 2 chromic catgut. The area was irrigated with tincture of merthiolate and the open laceration was filled with sulfanilamide powder. The laceration was then closed with eight interrupted No. 2 chromic catgut sutures.

Postoperatively, the patient's course was uneventful. Penicillin, 20,000 units every four hours, and sulfadiazine, 1 Gm. every four hours, were given for three days. Two days after operation, hemoglobin was 9.2 Gm., 54 per cent; red blood cells, 3,350,000; white blood cells, 6,000. The temperature rose to 101.8° F. on the day after operation, followed by a nonmorbid course during the remaining six days in the hospital. Subsequent examination on Oct. 31, 1945, in the office revealed a well-healed laceration, and the patient had no complaints.

Absorbable gauze also proved to be of value during vaginal procedures. As has been pointed out, it sometimes proved to be ineffective when applied to the oozing incision of completed plastic operations. Its inability to control such bleeding cannot be regarded as a failure, but as a faulty application. The gauze must be placed in direct contact with the bleeding vessels under temporary or permanent pressure to cause hemostasis. On the other hand, absorbable gauze was used effectively during the course of a plastic operation to check oozing not readily controlled by ligature. It was effective in controlling hemorrhage from biopsy wounds and from the crater of a carcinomatous cervix. The most valuable application of this material noted in this series of cases was in a group exhibiting violent secondary hemorrhage some days after a plastic operation, a cervical amputation, or a complete hysterectomy. Absorbable gauze placed against the source of hemorrhage and held in position with plain packing promptly controlled such hemorrhage. Formerly plain packing usually proved ineffective under such circumstances, necessitating ligation of bleeding vessels and resuture of the disrupted area under conditions of difficult exposure. The use of absorbable gauze in such cases appeared to offer great advantages.

### Conclusions

1. Absorbable gauze has been utilized in 30 gynecologic patients to control hemorrhage. Among these cases, there was an equal number of abdominal and vaginal procedures.

2. When properly applied, it was uniformly effective in controlling hemorrhage.

3. No reaction was observed attributable to the presence of absorbable gauze in closed cavities.

4. It was particularly useful in the control of secondary vaginal hemorrhage.

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### Discussion

DR. WILLIAM E. STUDDIFORD.—In reply to a question Dr. Studdiford stated that absorbable gauze has been packed into the cavity of the uterus of an experimental animal through a hysterotomy incision. It was absorbed without any remarkable reaction. It has not been packed into the human uterus by the vaginal route. The certainty of bacterial contamination, its amorphous character after being in contact with blood and serum, and the consequent difficulty in its removal have made such a procedure seem a matter connected with considerable risk.



However, Moensch, in 1927, had reported a death from air embolism following the insufflation of the tubes with atmospheric air. Other cases have been recorded, as noted by W. F. Finn.<sup>3</sup> The use of carbon dioxide to avoid this danger demanded more elaborate equipment, and the availability of the gas in tanks. This complication seemed to make Jacoby's simple apparatus disapproved.

In an effort to overcome this objection, a suction flask (1, in Fig. 1) has been cut into the tube from the cannula (3) to the manometer (3). In this flask is placed a heaping tablespoonful of sodium bicarbonate. A separation funnel (2) is attached to the mouth of the flask through a rubber cork. In this funnel is placed citric acid; about 10 per cent. The flask should hold about 600 c.c.; and the funnel has a capacity of 200 c.c. By means of the stopcock (5) at the base of the funnel, the acid is dripped upon the sodium bicarbonate. When the air has been displaced from the whole system, carbon dioxide may be proved to be coming from the cannula tip (6) by immersing that in a small glass containing lime water, and noting the milky reaction. With the finger closing the cannula tip, the piston of the syringe is drawn out slowly, filling the barrel with carbon dioxide from the flask. It will be noted that the acid in the funnel acts as a valve to prevent too much pressure of carbon dioxide forming in the flask. With the finger over the hole in the end of the cannula, bubbles of carbon dioxide pass upward through the funnel. Never allow the funnel to become entirely empty. In pulling out the piston to fill the syringe, it is important to go just fast enough to prevent the rise of these bubbles in the funnel and not fast enough to run any risk of drawing atmospheric air into the system. A sterile clamp is now snapped on the side tube (7) leading from the flask to the "T" tube (8) which connects with both manometer and cannula. The tip of the cannula is now placed in the cervical os and the test is carried out as directed by Jacoby. Of course, the pressure that does the test is obtained by gently pushing in the piston of the 30 c.c. syringe (9). Meanwhile, carbon dioxide still forming in the flask simply bubbles off through the remaining acid in the funnel. By removing the clamp and repeating the filling of the syringe, the test may be tried again.

This method may be used in connection with a simple small-sized female catheter made of metal, and carrying a cone-shaped rubber sleeve near the tip. Such an outfit is much less convenient; but might be employed if the Jacoby cannula is not available. Also, the technique may be varied by placing Seidlitz powder (sodium bicarbonate and tartaric acid) in the flask and dripping simple water from the funnel. However, in this method, it seems less easy to control the rate of generation of the carbon dioxide.

### Summary

A simple apparatus for the insufflation of the Fallopian tubes is described. Carbon dioxide for the test is generated, thus eliminating the need for tanks or other source for the gas.

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## SIMPLIFIED APPARATUS FOR INSUFFLATION OF THE TUBES WITH CARBON DIOXIDE

JOSEPH T. SMITH, M.D., BOSTON, MASS.

(From the Joseph H. Pratt Diagnostic Hospital)

IN THE work of the Bingham Associates Fund designed to help physicians and hospitals in small communities, it is the constant effort to discover and develop methods of performing modern diagnostic tests in the simplest and cheapest manner possible consistent with the highest standards of safety and accuracy.

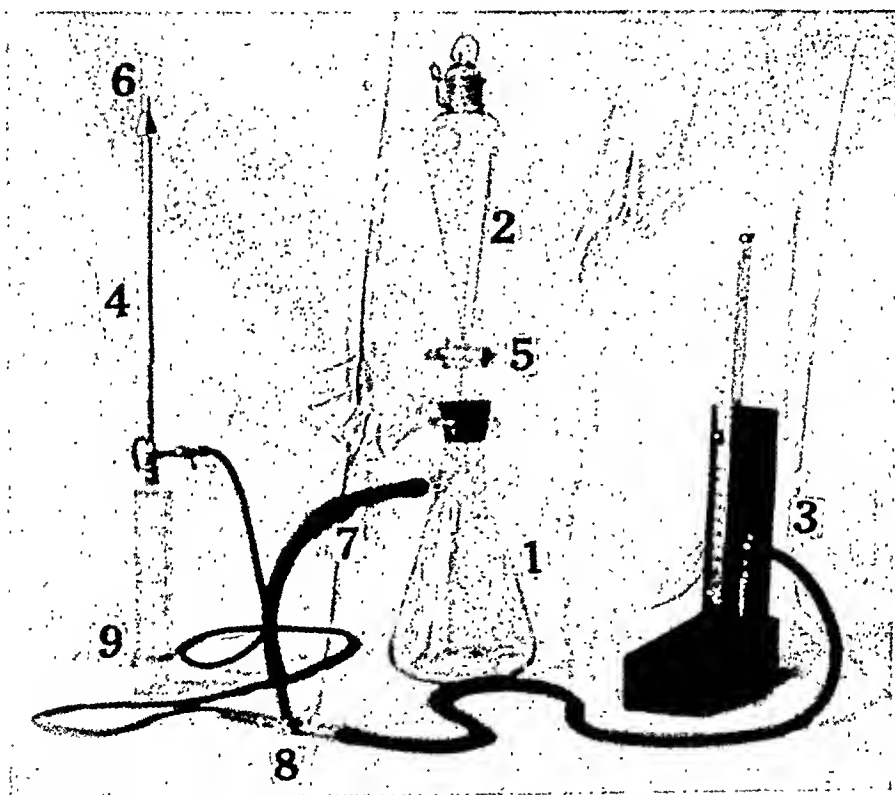


Fig. 1.—Tube insufflation Apparatus. (1) Flask for sodium bicarbonate; (2) funnel for acid; (3) manometer; (4) Jacoby insufflation cannula; (5) stopcock; (6) cervical tip of cannula; (7) clamp; (8) "T" connection; (9) 30 c.c. syringe.

A case in illustration is the Rubin test for patency of the Fallopian tubes. It is illogical to require a patient who would benefit from such a test to have to go to the expense and waste of time required for a trip to one of the larger medical centers, with hospitalization there. Yet the small rural hospital and the country doctor are not usually equipped with elaborate apparatus for the making of such a test. So, some years ago, we were interested in the syringe and cannula suggested by Dr. Jacoby.<sup>1\*</sup> This device works simply and well; and seemed ideal for the physician who wished to perform only a few such tests a year. Jacoby's suction eurette<sup>2</sup> could be used with the same syringe, thus giving a doctor valuable diagnostic equipment for a small outlay.

\*Manufactured by Becton, Dickinson & Co.

I believe that the following are the advantages of the new introducer and cannula:

1. The instruments are extremely simple to use. Even the operator having limited experience in continuous caudal analgesia finds them easy and convenient to handle.

2. There is a definite lessening of the possibility of infection.

3. There is less possibility of piercing the rectum, vagina, and the unborn infant.

4. The introducer makes a semicircular door opening in the skin and subcutaneous tissues, which acts on the same principle as the double-hinged door; and is pushed open by inserting the cannula, closed by withdrawing it, and sealed by the serosanguineous fluid.

5. The cannula is less likely to pierce the dural sac than the ordinary needle or catheter with a stilet.

6. The possibility of breaking the cannula is almost nil. It is made of annealed stainless steel. Furthermore, the round pointed cannula cannot become imbedded in any tissue.

7. In 95 per cent of all cases, the sacral canal is easily located and caudal analgesia administered successfully.

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# A NEW INTRODUCER AND CANNULA FOR OBSTETRIC AND SURGICAL CASES SUITABLE FOR CAUDAL ANALGESIA

J. ROY COMPTON, M.D., ST. LOUIS, MO.

NUMEROUS modifications of the Hingson and Edward procedure for continuous caudal analgesia and anesthesia have been reported since the publication of their methods in 1942. Prominent among these variations has been the use of the 13-gauge spinal needle for reaching the caudal canal, followed by inserting an ureteral catheter through the needle into the canal.

In the March 1, 1944, issue of the *Journal of Missouri State Medical Association*, I described a procedure employing the Hingson needle. This procedure, termed "The Original Pressure Point Technique for Insertion of the Caudal Needle," was highly successful. Following publication of this article, and as a result of experimentation, I perfected an introducer and cannula of a new design which made the pressure point technique still more effective. The new type of introducer and cannula is shown in Fig. 1.

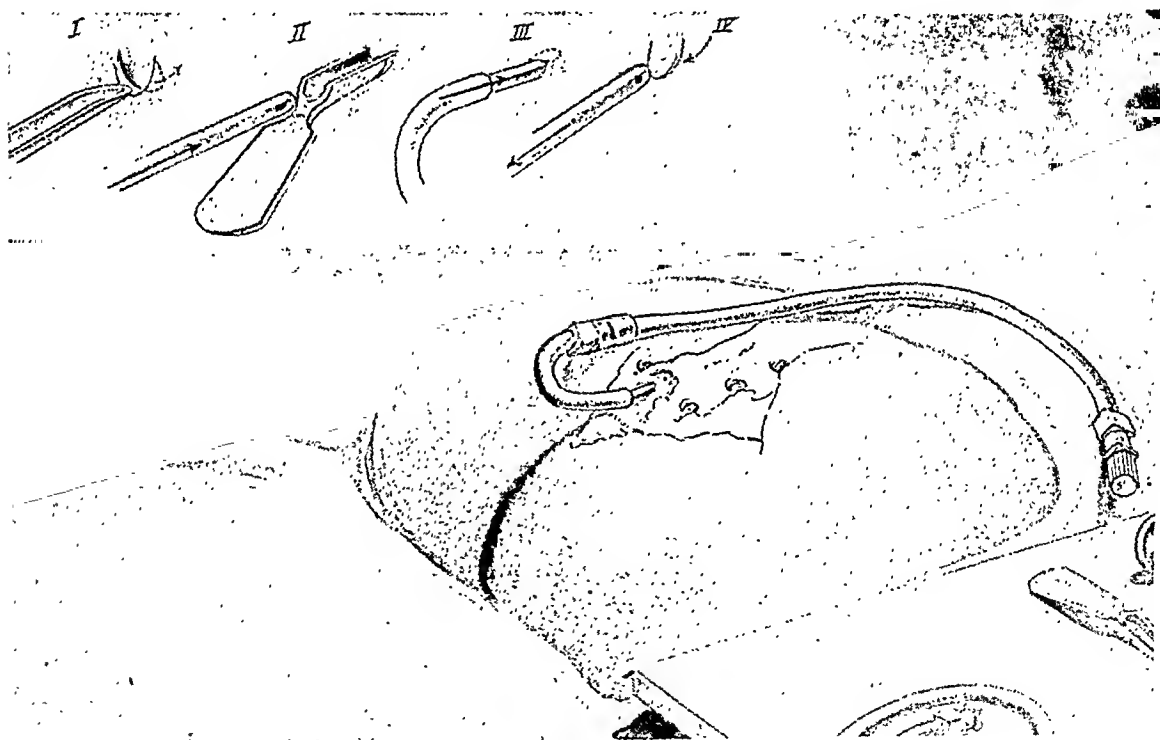


Fig. 1.

The Compton caudal introducer is a semicircular introducer with an easy-to-grasp handle, is 13 gauge,  $2\frac{1}{2}$  inches long, made of stainless steel, with a short bevel to carry the Compton cannula or a No. 6 ureteral catheter. The Compton caudal cannula is a No. 5 French cannula,  $2\frac{1}{2}$  inches long, made of stainless steel, with a round end and bilateral fenestra. With short tubing and adapter, the overall measurement is five inches.

## RETENTION CATHETER

WILLIAM T. KENNEDY, M.B. (Tor.), L.M.C.C., F.A.C.S., New York, N. Y.

(From the Clinic of Woman's Hospital)

**M**ANY gynecologists would use a retention catheter following plastic operations, providing the catheter would satisfy certain rigid requirements, among them that: (1) The patient must be almost unaware of its presence;

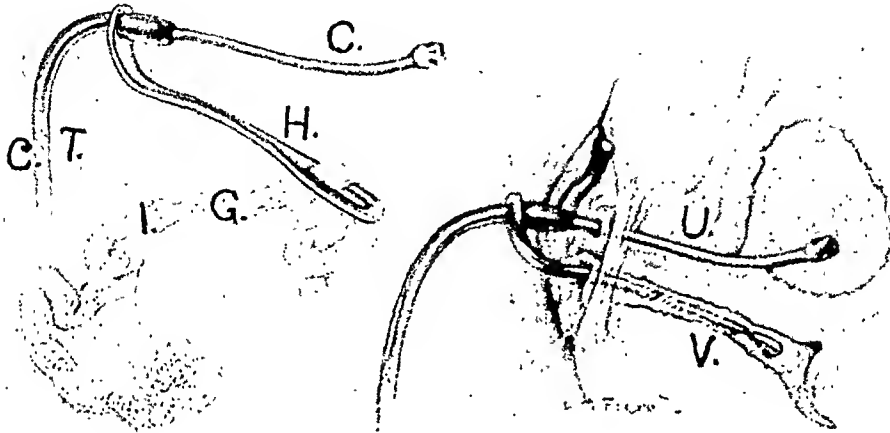


Fig. 1.—Illustration of the assembly of the catheter, holder, iodoform gauze, and connecting tube, before and after placement. C. = Catheter (vitalium). H. = Holder (vitalium). C.T. = Connecting tube, rubber. I.G. = Iodoform gauze. V. = Vagina. U. = Urethra.

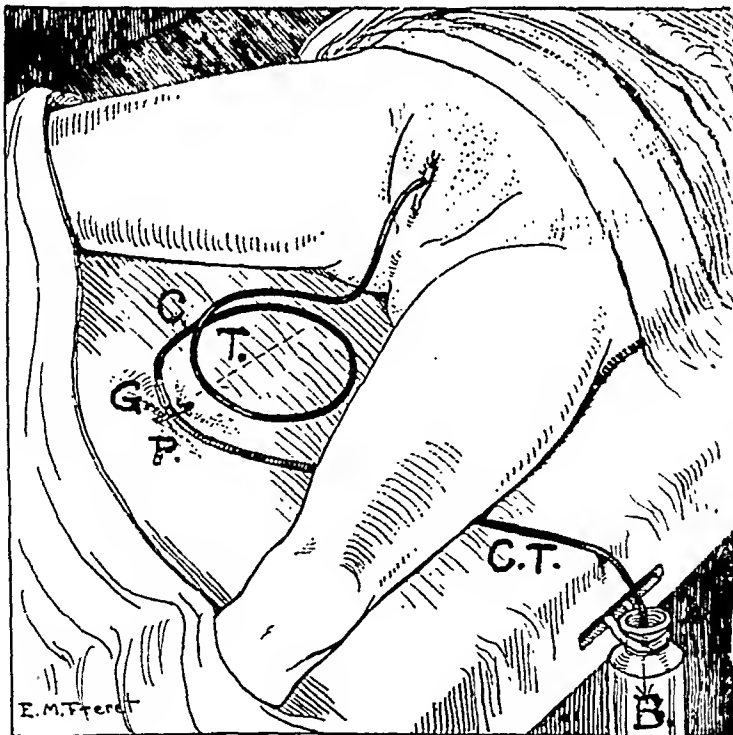


Fig. 2.—Illustration of a patient on the bed to show how the catheter should be placed. C.T. = Connecting tube, rubber. P. = Pin to keep the end of the connecting tube in the middle of the bed. This allows the patient free movement without traction on the catheter. G. = Glass connecting tube. B. = Bottle into which urine runs.

# AIR CYSTOSCOPE WITH A UNIVERSAL HANDLE AND EXTERNAL LIGHT\*

BENJAMIN LEFF, M.D., PHILADELPHIA, PA.

(From the Department of Gynecology, Mount Sinai Hospital)

THE light in this scope is attached to the handle outside of the bladder. It is derived from a flashlight bulb and is reflected into the viscus through the cystoscopic tube by means of a ground lens. A small adapter, for the cord

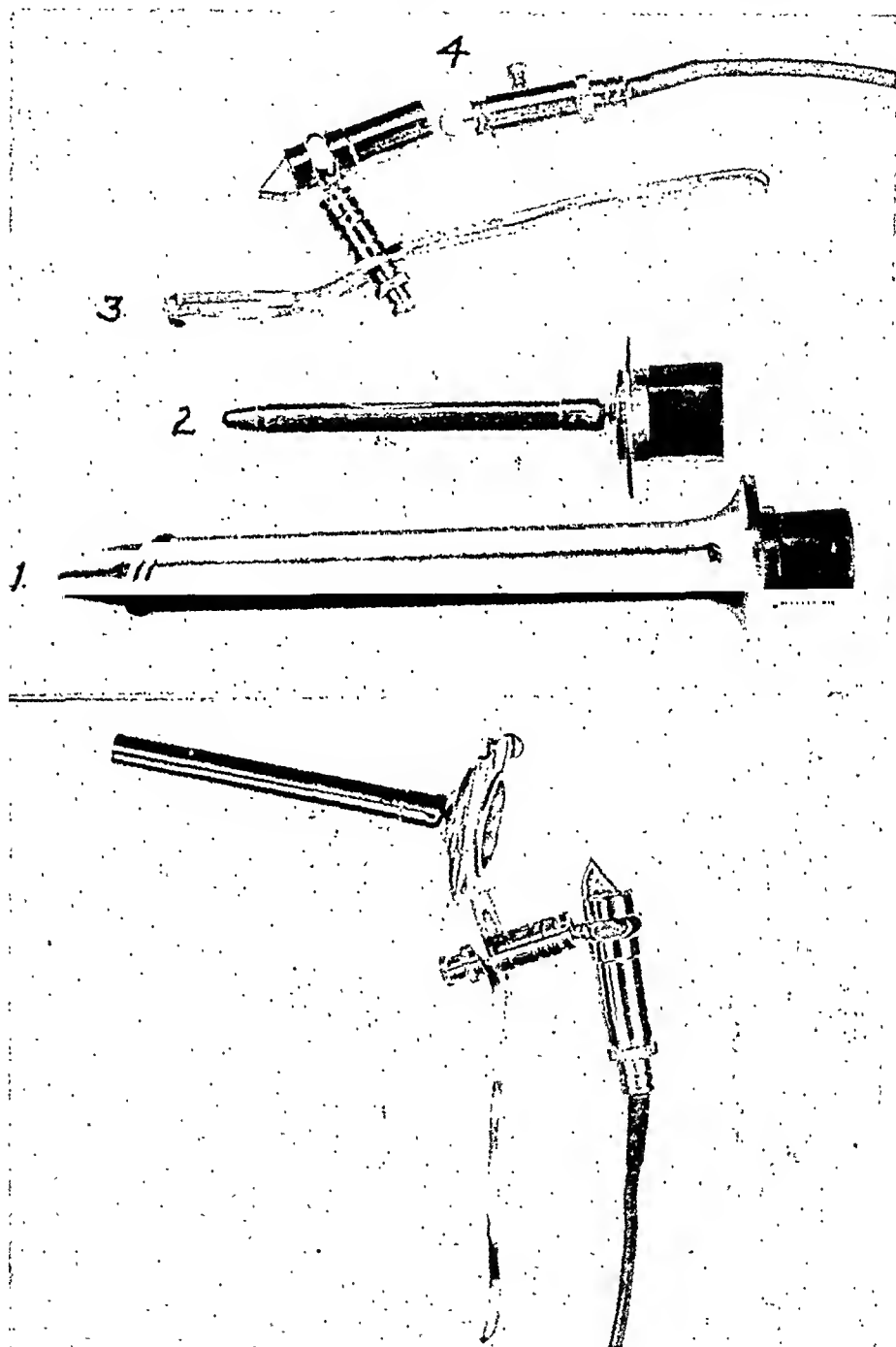


Fig. 1.—(1) Proctoscope attachment; (2) cystoscope attachment; (3) universal handle; (4) light carrier.

Fig. 2.—Assembled cystoscope (obturator removed).

terminals, inserted into the socket of a flashlight battery eliminates the necessity for a rheostat. In addition, this scope has a universal handle. Tubes for examining other body cavities may be made and used interchangeably with this handle.

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\*This instrument was assembled by the Martin Medical Company of Philadelphia from parts made by the National Electric Instrument Company of Long Island, New York.

## SEE-SAW RESUSCITATOR FOR THE TREATMENT OF ASPHYXIA IN THE NEWBORN

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NEW YORK, N. Y.

SOME months ago, when one of us was confronted with a case of asphyxia in a premature infant weighing approximately 4 pounds, the various available means for resuscitation were discarded for the following reasons: (1) Mechanical respirator—the use of this would expose the small child to chilling, and

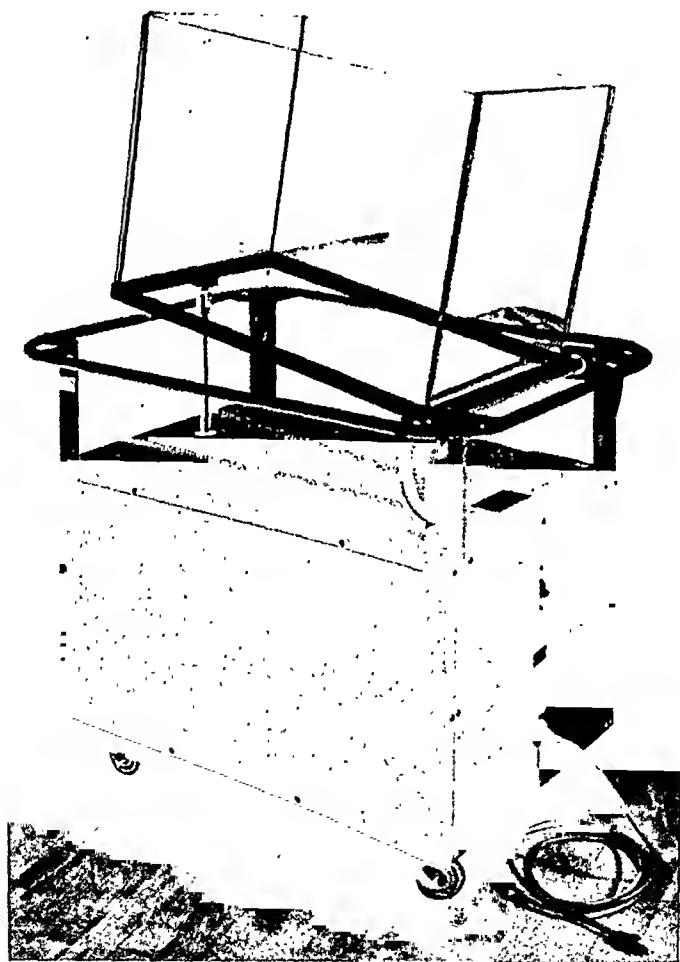


Fig. 1.

trauma might follow the initial application of the respirator. (2) Mouth to mouth insufflation—because of the possibility of pulmonary infection in the immature child.

Therefore, the see-saw method, described by Frank C. Eve, in the *Journal of the American Medical Association*, 124: 964, 1944, was used. In this method the position of the body is alternated frequently by rocking on a trestle, so as

(2) the skin of the mons, the labiae, and the perineum and the skin of the legs must remain clean; (3) there must be no traction in any direction on the labiae; (4) the patient must be able to have normal bed locomotion without disturbing the catheter; (5) the catheter must keep constantly clean for several days and not require any routine irrigation; (6) there must be no need to change or replace the catheter; (7) the catheter must absolutely abolish all need of catheterization, and (8) exasperating and discouraging complications after operation caused by frequent passing of an ordinary catheter are less apt to occur.

The author presents such a catheter\* made of vitallium, the nonelectro-active nonirritating alloy which has been used in human tissue without any evidence of corrosion. The author has used this catheter for more than three years and has never had one corrode or become stopped. Should evidence of cystitis, trigonitis, etc., be manifest, the tube may be separated at the glass-connecting tube and the bladder irrigated without removing the catheter. Bleeding should be stopped from vaginal incisions following extensive plastic vaginal operations, fistula operations, and operations for incontinence. If the holder is then inserted and loosely packed with iodoform gauze, the gauze will remain uncontaminated for a week or more. The average length of time the author leaves the catheter in is seven to ten days. It can easily be removed and will retain the same glossy metallic surface. The incisions, which have been undisturbed during the time the catheter has been in place, will have quite firmly united and there will have been no trauma to urethra or bladder, even by the retention catheter.



## Special Article

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### GOVERNMENT SPONSORSHIP OF A MATERNITY PROGRAM IN WARTIME

#### Can It Be Successfully Perpetuated in Peacetime?

CAPT. PHINEAS BERNSTEIN, COMDR. FERDINAND J. SCHOENECK, AND

LT. COMDR. HERBERT ZERNER, M.C., USNR

*(From the United States Naval Hospital, Newport, Rhode Island)*

**T**HIS report of 500 consecutive pregnancies may have special significance at this time, since it presents facts and impressions of a Maternity Clinic under government control in medicine. All statistics and opinions contained herein pertain to the Family Clinic of the United States Naval Hospital at Newport, Rhode Island, during the years from 1941 to 1944.

Patients were hospitalized at the Newport Hospital (civilian), since facilities for the care of dependents were not available at this naval activity. Professional care, however, was rendered exclusively by Naval Medical Officers, all of whom were formerly civilian physicians.

Excellence of maternity care and maximum protection for the parturients were attained through the close cooperation of the clinic's qualified obstetricians with a group of specialists on duty at the Naval Hospital proper. The assistance rendered by this latter group proved indispensable for the proper treatment of many nonobstetric complications. The extended hospitalization and increase in medical attention required for these complications assumed a striking significance, since they radically altered our generally accepted concept of maternity cost.

Since all aspects of a government maternity program, in its essential structure, have been experienced, conclusions which may be of value in considering the problem of government medicine may be clearly set forth. A brief discussion and presentation of carefully collected data seems warranted.

For purposes of analysis, the program as carried out will be considered in two categories, namely, (1) obstetric care and (2) economic aspects.

#### Obstetric Care

Prenatal, natal, and postnatal care were rendered in accordance with the maximum standards as adopted by eminent and authoritative modern obstetric centers. All patients received routine lung x-rays and, when necessary, roentgen films (36.4 per cent) were employed for pelvimetry. A complete laboratory checkup, including Rh factor determination, was performed on each patient. Especially emphasized was history taking and diagnosis of presentation and position of the fetus during the six weeks before the onset of the expected labor. Care during labor and delivery was on a level with that established in recognized obstetric organizations. The majority of cases were delivered by diplomates of the American Board of Obstetrics and Gynecology and, in instances where patients were not delivered by qualified specialists, a very close supervision supplemented by teaching of the younger staff physicians was rendered by these specialists.

to allow the weight of the liver and abdominal contents to drop downward, and thus pull air into the lungs when the head is raised and the feet lowered; and the reverse to take place, causing expulsion of air from the lungs when the head is lowered and the feet raised.

The child's head was lowered, and immediately the familiar thick mucous plug was expelled through the child's nostrils. Alternate rocking of the child transferred and removed the weight of the abdominal viscera to the diaphragm, and thereby established a nontraumatic pulmonary ventilation.

The apparatus pictured in the illustration consists of a lucite box, opened at the top and sealed at the edges and the bottom, resting on a platform which has a fixed level at one end, and at the other end is attached to a rod connected to an electric motor, placed in the bottom of the cabinet that raises and lowers that end of the box a given number of times per minute. This can be altered from the usual rate of forty per minute by a simple change of a lever arm on the motor. The lucite box which is shown in the illustration, without the usual baby's mattress in place, is shatterproof, and has sufficient depth to permit the flooding of it with oxygen through the opened end of the box, and to take advantage of the fact that the increased molecular weight of oxygen over that of atmospheric air will have the concentration of oxygen down close to the baby. Furthermore, it is permissible to make any necessary examinations on the baby, or carry out the further aspiration of mucus, or the use of stimulants through the opened top. Heat can be supplied from electric blanket or hot water bag. It is advisable to aspirate as much mucus as possible with the first lowering of the baby's head before the head is elevated, which tends naturally to make the baby aspirate the mucus itself.

TABLE III. RECORD OF ALL MEDICAL VISITS IN 500 PATIENTS AND NEWBORN

	TOTAL	AVERAGE PER PATIENT
a. Prenatal visits (Table II)	4,529	9.06
b. Hospital delivery visits (500 cases)	500	1.00
c. Hospital postpartum visits 10 days for 500 mothers and 490 infants	9,900	10.0
d. Consultants visits, nonobstetric medical and surgical consultations only (Table IV)	102	0.10
e. Additional hospital visits by clinic staff for complications, after usual 10-day period (Table IV)	4,450	4.50
a. Maternal (Table IV a) 2984 - 5.92 ea. (Table IV b) 1466 - 3.20 ea.		
b. Infants	Total 4450—9½ visits per patient	
f. Home visits made during pregnancy	118	0.24
g. Clinic visits for postpartum checkups one per month for 4 months	2,000	4.00
Grand total	21,599	28.90

included are the prenatal and postnatal visits for eight (1.6 per cent) tubercular patients (diagnosed by routine chest films) who actually were visited by attending physicians at the Wallum Lake Tuberculosis Sanatorium, where they were hospitalized prior to and after delivery. The increment of both medical visits and hospital bed days for the treatment of these eight tubercular patients was preponderantly large.

Table IV indicates not only the diseases complicating the pregnancy and neonatal periods, but also the hospitalization and the professional visit increase incidental to them. The textbook variety of diseases, so strikingly paralleled by this group of complications, implies the valid and forceful admonition that an obstetrician and gynecologist, no matter how well trained, must depend on the advice of medical and surgical specialists if the patient is to receive adequate advice and treatment.

Sixty-nine (13.8 per cent) of the mothers were hospitalized for the more serious of 421 ailments noted in Table IV; their treatment required an additional 2,984 hospital days, or an equivalent of 60 per cent of the usual lying-in period for 500 normal parturients. Similarly, the 43 complications of the newborn babies required 1,466 extra hospital days, an increment of 30 per cent over the in-hospital period ordinarily required for 490 viable infants. These complications, furthermore, increased the medical visits of both staff members and specialists by 4,552 calls (21 per cent).

The obstetric costs, based on conclusions drawn from this data (Table IV), must therefore include an increase per capita of six days for the maternal hospitalization, and of three days for that of the newborn. Combined, these represent an over-all increase of 45 per cent in the basic obstetric cost. In addition to this, these complications increased the potential professional cost by 21 per cent.

While 80 per cent (362) of all maternal and newborn complications could be satisfactorily treated by the clinic staff, the remaining 20 per cent (102) required the services of numerous specialists. These included medical, surgical, eye, ear, nose and throat, skin, lung, and x-ray specialists, as well as neurologists, cardiologists, urologists, psychiatrists, orthopedists, and pathologists. In all, 102 nonobstetric consultations were made (Table IV). It is our confirmed opinion that a staff of this character constituted a definite safety factor for the large number of patients cared for in this clinic.

Although not referred to in Table IV, there were numerous obstetric complications which necessitated specialized attention, but the postpartum hospital-

TABLE I. STATISTICS IN 500 CONSECUTIVE DELIVERIES

Vaginal deliveries			486	97.2%
Cesarean sections (5 secondary sections)			14	2.8%
Forceps deliveries			307	61.4%
prophylactic	263	52.6%		
extractions	44	8.8%		
Episiotomies			388	77.6%
Maternal mortality			0	0
Maternal morbidity				3.2%
Fetal mortality (gross)				5.7%

The excellent results obtained reflect the merits of scientific obstetric care and modern methods. Table I presents a record of clinical facts which, in our opinion, speaks for itself.

### Economic Aspects

To determine the general economic picture as applied to this clinic, a quantitative study of several elements of the program was necessary. These included the determination of the number of days of hospitalization, number of medical visits, obstetric, medical, and surgical consultations, and the complications of pregnancy. The attitude of physicians as well as the patient was also examined in pertinent detail. Additional features, such as social service, financial aid, and home aid and nursing are discussed.

There were 4,529 prenatal visits made by 500 patients. Many were seen for comparatively short periods since their husbands' "orders" required moving from one station to another. Table II indicates the statistical record of all prepartum clinic visits.

TABLE II. PRENATAL ATTENDANCE OF 500 PATIENTS

NO. OF VISITS	NO. OF PATIENTS	TOTAL
12	101	1212
11	88	968
10	78	780
9	75	675
8	39	312
7	41	287
6	18	108
5	22	110
4	5	20
3	14	42
2	6	12
1	3	3
0	10	0
	500	4529

In order to ascertain the total number of medical visits required for the complete care of these patients, the following statistics were prepared: Table III presents an over-all quantitative analysis of the care furnished by all physicians in attendance, and includes visits made by obstetric, medical, and surgical specialists, as well as other medical staff members, for both mother and baby.

The average of 28.9 physicians' visits per patient represents all medical calls made. On the basis of the customary ten-day postpartum hospitalization period, the 500 parturients and the 490 viable infants required 9,900 hospital days. The complications which occurred actually increased this normal hospitalization period 41.0 per cent. It should be noted that nursery visits are recorded individually and separately from calls made upon mothers, since the newborn were under supervision of a medical officer assigned as a pediatrician. Also

ization requirements for these were not materially increased. These included three placenta previas, one abruptio placenta, one brow presentation, several toxemias of pregnancy (one, a breech presentation), four instances of cephalopelvic disproportion delivered by cesarean section after trials of labor, five instances of postpartum hemorrhage, and four retained placentas. Several major surgical procedures were also necessary for acute abdominal conditions which occurred during pregnancy.

The program, in addition to the medical care outlined, included many other features, which, in our considered judgment, were essential to its success. These, we submit, must be continued if a complete and satisfactory program is to be maintained during peacetime. The Emergency Maternity and Infant Care Program of the Federal Government defrayed the costs of war hospitalization in 58 per cent of our cases; the remaining 42 per cent paid their own hospital bills. All other care and service was rendered without charge.

The Emergency Maternal and Infant Care plan functioned smoothly under a special Rhode Island State Agency. However, several criticisms of this plan will be discussed. Applications for this service were prepared and investigated by the local Social Service nurses, or the Navy Relief Society representatives.

Further assistance was rendered by the Navy Relief Society and the American Red Cross for the varied problems which arose among many of the families in the lowest income groups of enlisted personnel. This included financial loans and outright gifts, temporary placing of children with responsible guardians, children's playgrounds, donation of clothing and layettes, Red Cross ambulance transportation, obtaining proper living quarters, and many other similar services.

The Rhode Island State Health Department furnished additional practical instructions for both mother and child, which, although overlapping our own services in certain respects, were of great assistance. Its specially trained registered nurses visited patients in their homes, attended minor medical complaints, furnished prescribed medications and treatments, and aided in problems of child feeding and care, and finally rendered not only nursing, but even housework assistance to the postpartum patient in need of help.

Notwithstanding the satisfactory clinic record of obstetric achievement and the excellent service rendered by these supplementary agencies, certain concrete and justifiable objections to this government Maternity Service were encountered. While it is felt that many of these were due to wartime conditions, some are existent in peacetime, and are presented as real and practical considerations.

Primary among the criticisms was the patients' continuously mentioned objection to the lack of what is ordinarily termed patient-physician relationship. At clinic visits patients were not uniformly seen by the same physician, nor was there any assurance that a certain doctor would be responsible for a specific delivery. The doubt as to which physician would actually perform delivery created a profound sense of insecurity in the patient's mind. This sense of insecurity was enhanced by the frequent change and occasional dearth of medical personnel which resulted in long periods of waiting, crowded clinics, hasty interviews, and attendance by new or different medical officers, all of which represented further justifiable causes of dissatisfaction. An intense resentment was generally expressed and obviously manifested toward ward hospitalization because of the attendant lack of privacy, disturbed rest, and impersonal nursing care. These complaints often resulted in insistence on private room accommodations at the patient's own expense—a grievance of serious import to the low income patient.

The opinion was, furthermore, often expressed that the parturients accepted these unsatisfactory conditions since "most of the specialists were in the service."

TABLE IV. DISEASES AND CONDITIONS FOUND IN 500 MOTHERS AND NEWBORN  
(Number, Consultations, Number Hospitalized and Total Hospital Days)

NUMBER	CONSULTATION	TYPE CONSULTANT	NUMBER HOSPITALIZED	DISEASE OR CONDITION	AVERAGE HOSPITAL DAYS	TOTAL HOSPITAL DAYS
<i>A. Maternal</i>						
12	1	Med	1	Hypertension without toxemia	3	3
8	2	Med	2	Hypertension with toxemia (vertigo, edema, tachycardia, negative urine)	15	30
8	3	Med	3	Phlebitis, femoral (2), saphenous (1)	15	45
6	6	Med	2	Diabetes mellitus	5	10
5	4	Med	5	Syphilis; treated with penicillin, and mapharsen and bismuth	7	35
4	3	Med	1	Asthma	8	8
3	3	Med	3	Preeclampsia; nephritis, hypertension, tachycardia	40	120
3	2	Med	1	Thyrotoxicosis	21	21
1	1	Med	1	Virus pneumonia	22	22
2	1	Med	1	Malnutrition	10	10
2	2	Med	2	Duodenal ulcer, active	19	38
2	1	Med	1	Catarrhal jaundice	24	24
1	1	Med	1	Pulmonary embolism	43	43
5	5	Heart	5	Decompensated rheumatic heart disease	28	140
1	1	Heart	1	Active rheumatic fever; gallop rhythm	36	36
4	4	Heart	0	Compensated heart disease; inactive (3 rheumatic, 1 congenital)	0	0
2	1	Heart	1	Tachycardia persists	12	12
8	8	Lung	8	Active pulmonary tuberculosis, sanatorium care	270	2,160
38	22	ENT	1	Upper respiratory infections, acute type	5	5
6	4	Ortho	2	Myositis, sprains, sacroiliac, lumbar, cervical, extremities	8	16
1	1	Ortho	1	Sciatica	22	22
3	2	Npsy	2	Psychosis (2 postpartum: 1 manic depressive)	15	30
1	1	Proct	0	Colitis, fistula	0	0
3	1	Urol	1	Unilateral kidney (postoperative status)	4	4
2	1	Skin	0	Ichthyosis	0	0
2	2	Neuro	2	Mild convulsions postpartum; 1 toxemia; 1 unknown etiology	6	12
1	1	Eye	1	Internal strabismus; surgical correction	4	4
1	1	Surg	1	Inguinal herniorrhaphy	10	10
91	0	—	4	Nausea, vomiting—first trimester	3	12
58	0	—	0	Extremity edema, severe	0	0
53	0	—	0	Pregnancy anemia	0	0
19	0	—	2	Uterine retroversion, symptomatic; first trimester	8	16
18	0	—	0	Obesity	0	0
14	0	—	4	Habitual abortion	8	32
12	0	—	0	Trichomonas vaginalis	0	0
4	0	—	2	Acute pyelitis; 1 bilateral	10	20
4	0	—	4	Gonorrheal cervicitis, Bartholinitis, urethritis; penicillin cure	3	12
4	0	—	1	Acute tonsillar abscess	6	6
4	0	—	1	Oophorectomy; twisted dermoid cyst	14	14
3	0	—	1	Uterine fibroids: 1 degeneration, conservative treatment	12	12
1	0	—	0	Measles	0	0
1	0	—	0	Chronic alcoholism	0	0
421	85		69			2,984
<i>B. Fetal</i>						
1	1	ENT	1	Congenital laryngeal stridor	120	120
8	0	—	8	Premature babies between 3 and 4 pounds	39	312
18	0	—	18	Premature babies between 4 and 5 pounds	18	324
6	6	Heart	6	Congenital cardiac anomalies	25	270
6	6	X-ray	6	Congenital duodenal stricture	20	120
2	2	X-ray	2	Enlarged thymus	10	20
2	2	Neuro	2	Hydrocephalus, spina bifida	150	300
43	17		43			1,466
464	102		112	Grand total: Maternal and fetal complications		4,450

Larger communities throughout the country, while in need, perhaps, of financial aid for needy cases, admittedly require no change in the type of high caliber obstetric service which is rendered by civilian organizations. In the smaller communities, however, there is a dire need for improvement, and it is highly dubious, in our opinion, as to whether a national plan of this kind will find it possible to overcome an important and specific problem relating to the procurement of specialist staffs for these small communities. In the majority of small towns an obstetric, medical, and surgical staff of specialists, similar to the one described at this hospital, is without doubt unavailable as a general rule. That the success of any maternity group service is dependent upon such a staff is a certainty, in our opinion. How the government will solve this vital problem, and whether it can be solved, is beyond the scope of this paper.

A physicians' and specialists' salary schedule, much increased over that used during the war, and commensurate with medical qualifications and the level of earnings in private practice, will add a tremendous financial burden to the expenditures already referred to.

It is imperative that this government project attract high caliber physicians, if it is to endure; and it will be impossible to accomplish this without at least a fair salary schedule. It is difficult to comprehend how obstetric service of the high quality rendered by this clinic will be continued, when one reflects the most recent example of government medical compensation, namely the low standard of professional obstetric fees set forth by the E.M.I.C. for maternity care. Excellent obstetric care cannot possibly be rendered at this low compensation level.

In order that efficient and scientific obstetric care be continued, the government subsidized system would be obliged to absorb well-trained physicians from civilian medical centers. The present high type of medical education and research must therefore be partially subsidized but not interfered with.

Experience, and a review of past government performance, would seem to indicate clearly that any government subsidized enterprise cannot exist without political interference, and it is difficult to visualize a federal maternity program that will prove the exception.

We repeat that good obstetrics can and has been practiced in the maternity clinic of the Newport Naval Hospital under government sponsorship.

If a maternity program of national scope is to be launched and perpetuated, we submit on the basis of experience gained in this government clinic, that it must of necessity employ all the cardinal principles, and eliminate all of the shortcomings recorded above. The smaller communities must share its benefits since here especially does the need exist for better obstetrics. The stupendous financial responsibility imposed by a high-grade maternity service, as well as the widespread benefits toward the national health, must be presented to the nation.

Any political attempt to advance this program, which obscures the simple but costly requirements that, in our experience, have proved to be both necessary and equable for all concerned, would be manifestly misleading. Unless such a program is presented in its true light, is thoroughly understood, and willingly accepted, it would, in our considered opinion, soon fall into general disrepute and finally into complete disuse.

From the physicians' point of view, it may be stated that, while absolutely no interference was incurred from superior officers in the treatment of patients, policy necessitated the constant use of "proper channels" to expedite routine matters. Although this proved irksome and time consuming, the medical care of the patient was rarely disturbed. "Paper work," while minimal in this Dependents Unit, consumed a fair share of the Medical Officer's time, and preparation of extended and detailed reports often took precedence over actual medical duties.

Of interest and significance with regard to future employment of doctors by the government were the responses to a questionnaire submitted to the entire group of specialists at this activity; it revealed that their peacetime salary requirements were four to five times more than the remuneration received for their services during the war period. Furthermore, all but one physician were unwilling to continue in salaried positions of this type and preferred to return to private practice. This attitude toward government employment was decisive.

Certain additional impressions were gained by the authors which will be discussed from the standpoint of perpetuating a similar government program in peacetime. Although these are based solely upon observations made at this Naval activity, it is nevertheless felt that they are applicable to any government controlled group maternity service. Careful analysis and mature consideration have revealed the requisites as well as shortcomings which appeared in this government maternity program. It is felt that if the necessary conditions are fully met, a federal program based on these essentials might be successfully maintained.

While the implications as to the future success in peacetime of a similar undertaking of national scope are somewhat dubious in our minds, a review of the factors which proved essential to the success of this wartime clinic may prove advantageous.

Of primary importance is the fact that a scientifically adequate maternity service can be, and was, rendered under government sponsorship during the war in this clinic. The excellence of service was made possible by conditions which were largely due to the exigencies of the war period. These may be stated as follows:

1. An over-all medical and nonpolitical control exercised solely by a group of physicians; in this instance, the medical officers in charge of the Bureau of Medicine and Surgery of the United States Navy.
2. Complete and immediate supervision by specialists in Obstetrics and Gynecology unhindered by any nonmedical influence.
3. Cooperation of a large and varied staff of well-trained and qualified medical and surgical specialists.
4. Emphasis on prenatal and parturient care in accord with the highest precepts and doctrines of modern and scientific obstetric teaching.
5. The incorporation of an efficient and human Social Service, Home Aid and Nursing, and Financial Aid organizations, which completed the program at this activity.

These were the cardinal elements which, in our opinion, effected excellent care and a smooth and efficient clinical management of the program. The perpetuation of such a clinic after the war will be dependent upon these basic principles. In addition, the elimination of ward hospitalization, crowded clinics, impersonal nursing, insecurity of patients caused by doubt as to medical attendance at delivery, etc., are essential. The various minor extraneous duties imposed upon physicians should be transferred to proper extramedical departments. The above changes obviously demand increased expenditures, but they are absolutely necessary to achieve results compatible with a satisfactory service for patients and satisfactory working conditions for physicians.



ject. The book is well illustrated, particularly on the section on operative technique and postoperative cure. The completeness of the book is noted in a discussion on the social and economic conditions effecting this phase of medicine, which includes a section on the function of the medical social worker, and her part in the problems of Gynecologic Nursing.

PHILIP F. WILLIAMS

Van Ravensteyn has published a doctoral thesis from the University of Utrecht, containing studies on follicle ripening.<sup>5</sup> In the true doctoral fashion, he starts his bibliography with Hippocrates, and ends with Regnier de Graaf.

The book contains a careful study of the development of the ovarian follicle, influenced considerably by the work of Moricard. Besides the histologic data, he has investigated the vitamin C content of the follicular cells in the preovulatory phase. He concludes with reports on war amenorrhea.

R. T. FRANK.

This monograph deals with the iron metabolism of mother and child during pregnancy. The hemoglobin of the serum is elevated during pregnancy over that of the nonpregnant average, drops abruptly after labor, but within one week reaches the nonpregnant norm. The placenta acts as a supplementary spleen. This accounts for the increased hemolysis in pregnancy. Iron can traverse the placental barrier. The fetus' serum has a higher iron content than that of the mother. In the newborn, there always is a hyperbilirubinemia (indirect). If there is a reduction in blood volume, according to the author, jaundice develops.

R. T. FRANK.

The second edition of Barbosa's *Practical Obstetrics*, which, in 1940, was given the Mme. Durocher's prize, has appeared after an interval of four years. This is a very detailed, simple description of every phase of obstetrics, normal as well as pathologic. The exposition is very sequential and paragraphed in such a fashion as to be striking to the student or obstetrician. There are numerous illustrations, mostly schematic, simple, but very expressive. The additional new illustrations and the revision have brought the book fully up to date.

R. T. FRANK.

**Human Embryology** by Pattens is designed for the medical student and practitioner. The text aims to show the great practical importance that a knowledge of embryology plays in everyday medicine. The continuity of development, sequence, and significance are featured. The hormonal cycle, its change during pregnancy, and the consequent phenomena are described. False implantation, placenta previa, monsters, teratology, achondroplasia are some of the subjects introduced. This method of treatment keeps up interest and aids in remembering facts.

<sup>5</sup>**Studies Over de Follikelrijping.** Histologisch onderzoek over de follikel van de Graaf in de praevulatiephase, klinisch onderzoek over de oorlogsamennorrhoe te 's Gravenhage in 1944 en 1945, met een inleiding over de geschiedenis van het onderzoek van de follikel van de Graaf. Door Theodoor Leopold Willem Van Ravensteyn, Arts, Geboren Te Eerbeek. Proefschrift, Ter Verkrijging Van Den Graad Van Doctoor In de Geneeskunde Aan De Rijksuniversiteit Te Utrecht. Op Gezag Van Den Rector Magnificus Dr. J. Boeke, Hoogleraar In De Faculteit Der Geneeskunde, Volgens Besluit Van Den Senaat Der Universiteit Te Verdedigen Tegen De Bedenkingen Van De Faculteit Der Geneeskunde Op Dinsdag 5 Maart 1946. Des Namiddags Te 3 Uur. 127 pages. Eduard Ijdo N. V., Leiden, 1946.

<sup>6</sup>**Het Ijzermetabolisme Bij Moeder en Kind.** Door M. J. Renaer. 159 pages. Uitgeverij N. V. Standaard-Boekhandel, Antwerpen, Brussel, Gent, Leuven. 1945.

<sup>7</sup>**Obstetrícia Prática** (Laureada pela Academia Nacional de Medicina com o Prêmio Mme. Durocher de 1940). By Luiz Agulrre Horta Barbosa, Docente livre de Clínica Obstétrica e de Clínica Ginecológica da Faculdade Nacional de Medicina da Universidade do Brasil. Assistente da Maternidade Escola. Assistente de Ginecologia e Obstetrícia do Hospital de S. João Batista da Lagoa. Professor do Curso de Enfermagem Obstétrica. Membro da Sociedade de Obstetrícia e Ginecologia do Brasil, da Associação Paulista de Medicina e Cirurgia e da Sociedade de Obstetrícia y Ginecologia de Buenos Aires. 2.ª Edição. 518 pages. Editora Científica, Rio de Janeiro. 1945.

<sup>8</sup>**Human Embryology.** By Bradley M. Patten, Professor of Anatomy in the University of Michigan Medical School. 776 pages. With 1,366 drawings and photographs grouped as 446 illustrations, 53 in color. The Blakiston Company, Philadelphia. 1946.

# Department of Reviews and Abstracts

## Review of New Books

### Gynecology and Obstetrics

The third edition of the *Synopsis of Gynecology*<sup>1</sup> based on the textbook, *Diseases of Women* by the two Crossens, has appeared. This is the third edition since 1932. The book, like previous editions, contains a tremendous amount of information in very compact format, with quite a number of illustrations and plates. I notice that in this revision no mention of penicillin for the treatment of gonorrhea is made. This book is of value both as a review for students and as a handy reference for busy practitioners.

R. T. FRANK.

The ninth edition of Bourne's *Synopsis of Obstetrics and Gynaecology*,<sup>2</sup> since 1913, maintains the same object, namely, as a rapid review for passing qualifying examinations. It, likewise, is of real use to the busy practitioner.

The newer methods of therapy for functional troubles, as well as the use of the sulfonamides and penicillin for the treatment of gonorrhea, etc., are included. The footnote illustrations in line drawing are numerous and instructive. The book contains a huge number of facts within a small compass.

R. T. FRANK.

The 1945 *Yearbook of Obstetrics and Gynecology*,<sup>3</sup> edited by J. P. Greenhill, offers a quick and convenient résumé of the world's literature of the two specialties. As in the past, the personal comments of the editor regarding particular topics or individual papers lend much interest to the book.

PHILIP F. WILLIAMS

The third edition of *Gynecologic Nursing*<sup>4</sup> by Crossen and Hoffert follows closely the curriculum advised by the National League of Nursing Education. In the revision, the authors have noted the recent advancements of endocrinology, treatment of infection, preparation for operation and postoperative care, and the psychological factors involved in the sub-

<sup>1</sup>*Synopsis of Gynecology*. Based on the Textbook *Diseases of Women*. By Harry Sturgeon Crossen, M.D., F.A.C.S., Professor Emeritus of Clinical Gynecology, Washington University School of Medicine; Consulting Gynecologist to the Barnes Hospital, St. Louis Maternity Hospital, and St. Luke's Hospital; Fellow of the American Gynecological Society and the Central Association of Obstetricians and Gynecologists, and Robert James Crossen, M.D., F.A.C.S., Assistant Professor Clinical Gynecology and Obstetrics, Washington University School of Medicine; Assistant Gynecologist and Obstetrician to the Barnes Hospital and the St. Louis Maternity Hospital; Gynecologist to St. Luke's Hospital and to DePaul Hospital; Fellow of the Central Association of Obstetricians and Gynecologists. Third Edition. 253 pages. The C. V. Mosby Company, St. Louis, 1946.

<sup>2</sup>*Synopsis of Obstetrics and Gynecology*. By Aleck W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G., Consulting Gynecologist to the Samaritan Hospital, London; Obstetric Surgeon, St. Mary's Hospital for Women; Examiner in University of London; Member of the Central Midwives Board, and Conjoint Board of England. Numerous diagrams. 500 pages. Williams and Wilkins Co., Baltimore, 1945.

<sup>3</sup>*The 1945 Yearbook of Obstetrics and Gynecology*. Edited by J. P. Greenhill, Professor of Gynecology, Cook County Graduate School of Medicine. 503 pages, 114 illustrations. The Year Book Publishers, Incorporated. 304 South Dearborn Street, Chicago, Illinois. 1946.

<sup>4</sup>*Gynecologic Nursing*. By Robert James Crossen, Assistant Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine, St. Louis, and Frances W. Hoffert, Instructor, University of Minnesota School of Nursing, Minneapolis, Minnesota. Third Edition. 248 pages, 194 illustrations. The C. V. Mosby Company, St. Louis, 1946.

various electronic and nuclear forces, these are studied in connection with their linkage or disrapture. Then one ascends at the level of the greater aggregations, the giant molecules, organic chemistry, and further going-up to the colloidal, threadlike and leaflike units which form the fibrils and fibers, the films, membranes, and septa throughout living cells. The structure of protoplasm, the plasma membrane which is the interphase between living and non-living material; the submicroscopic architecture, changes in permeability. One of the main phases of the discussion is the myosin in muscles.

In addition to the senior author, Höher, various sections are taken up by Hitchcock, Bateman, Goddard, and Fenn.

R. T. FRANK.

**Diseases of the Adrenals** by Soffer<sup>11</sup> is a very compact but complete and thorough monograph on all phases of the adrenal gland. There is a short but detailed description of the chemical tests used in connection with adrenal diagnosis, particularly the determination of the sodium and chlorides in the serum and urine; likewise that of potassium and the assay for the male sex hormone and the 17-ketosteroids. The tests are completed by a description of the salt tolerance test, the salt deprivation test, and finally, perirenal insufflation. A short but adequate chapter deals with the physiology of the gland, including the effect on electrolytes, carbohydrate metabolism, and the secretion of the cortical hormone. The author takes up the relationship of the adrenals to all the other glands of internal secretion, a very complicated situation; likewise the effect of shock upon the adrenals.

The pathologic symptomatology and laboratory findings in Addison's disease are described in great detail, the author having a large clinical material with which to illustrate. A separate chapter deals with the treatment of Addison's disease, a very delicate situation which requires experience, laboratory control and minute attention to detail. Personally, I predict that the treatment of Addison's disease will become a specialty much like the treatment of diabetes has become. A chapter is devoted to the adreno-genital syndrome, both where it is purely functional, and where it is due to hyperplasia and malignant tumors. The very varied clinical manifestations are gone into in detail, including the effect on carbohydrate metabolism. The blood electrolyte changes in connection with hormonal studies are dealt with carefully. The final two chapters cover the subject of disturbances of the medulla.

This is a very well-balanced monograph written by a man who has a long personal experience with laboratory investigations and likewise a large clinical material which he has handled over a number of years. This monograph is to be highly recommended.

R. T. FRANK.

**Biological Actions of Sex Hormones** by Burrows<sup>12</sup> goes far beyond a mere compilation of the literature, although it covers the entire subject in a most detailed and masterly fashion. The author has a long experience in experimental work on the sex hormones, which has enabled him to present a huge bibliography in a most compact but yet accurate, full and well understandable form. It is quite impossible in the compass of the review to give even a faint impression of the immense amount of documentation, its excellent arrangement, and ease of finding. Naturally there are many omissions because the literature today is too great to permit of complete presentation, except in the form of an index medicus.

The hormones taken up are the gonadotropic ones, the gonadal hormones, both androgens and estrogens, the progestins, and finally the sex hormones of the adrenal cortex. This book should prove a standard source book for many years to come.

R. T. FRANK.

<sup>11</sup>**Diseases of the Adrenals.** By Louis J. Soffer, M.D., Adjunct Attending Physician, The Mount Sinai Hospital, New York City. Illustrated with 42 engravings and 2 color plates. 304 pages. Lea & Febiger, Philadelphia. 1946.

<sup>12</sup>**Biological Actions of Sex Hormones.** By Harold Burrows, C.B.E., Ph.D., F.R.C.S. 514 pages. University Press, Cambridge, London, England. 1945.

The newest ova—Hertig and Rock—are pictured. The ductless glands as a group, irrespective of embryonal development, are described.

The various systems are described, fully, clearly, as in other texts. The illustrations are abundant (1,366, with 53 in color), very well drawn and reproduced. A bibliography concludes this very satisfactory textbook.

R. T. FRANK.

The present volume, *Contributions to Embryology*,<sup>9</sup> from the Carnegie Institution of Washington, contains nine contributions. deAllenda, Shorr, and Hartman report the results of a comparative study of the vaginal contents of rhesus monkeys and women. These studies have revealed a fundamental similarity between the vaginal secretions in the two species, during the menstrual cycle and under the influence of exogenous hormones. The authors note that the vaginal mucosa of the monkey is thickest at ovulation, whereas the human, the epithelium is thickest in the luteal phase. Dr. Streeter contributes another section of his monograph, "Developmental Horizons in Human Embryos." In the current contribution, he discusses groups 13 and 14 of the 25 developmental groups which are to cover the first seven weeks of embryonic life according to the state of development. He has discussed the characteristics of the external form of embryos belonging to group 13, as well as fixed points in various systems in this age group. The period of indentation of the lens plate is an outstanding characteristic of group 14. The material for these studies has been contributed from many sections of the United States; such cooperation should be continued to forward this important work of the Institution.

Hertig and Rock contribute studies of two ova of the previllous stage having developmental ages of seven and nine days; and with Henser of two human embryos showing the earliest stages of definitive yolk sac. This material was discovered in surgically removed uteri. Wilson contributes the study of a sixteen-day (Rochester) ovum discovered in curettage material, and Marchetti describes a previllous human ovum, also recovered from a curettage specimen. This ovum was considered to be about thirteen days old. Corner discusses the development, organization, and breakdown of the corpus luteum in the rhesus monkey, and describes the appearances revealed by routine histologic methods. He notes that the diagnostic signs of the age of the corpus luteum of the monkey apparently can be applied to human corpora lutea. Burns contributes two articles on the reactions of the phallus and the urinogenital sinus in the opossum to sex hormones. He shows that estrogenic substances have an almost exactly opposite effect on histogenesis of the phallus compared with those produced by androgens. The reactions appear to be highly specific. His final contributions note the specific manner in which the tissues of the urinogenital sinus responds to treatments with androgens, a reaction which closely parallels the experiments described for the phallus.

PHILIP F. WILLIAMS.

### Miscellaneous

*Physical Chemistry of Cells and Tissues* by Höber with collaborators<sup>10</sup> is a serious and successful attempt to present "physiology as a branch of physical chemical science dealing with life as a physical, though exceedingly complex system, that may be subjected to scientific analysis like any other natural object." This is a presentation of the fundamentals and an analysis of the life of a cell by means of the tools of modern physics. In their preface the authors acknowledge that there are a great number of unsolved problems.

The book is far beyond the knowledge of the average physician unless he has had a good training in physical chemistry. Starting with the atoms and molecules and defining the

<sup>9</sup>*Contributions to Embryology*. Volume 31, numbers 195 to 206. 175 pages, illustrated, and 42 color plates. Carnegie Institution of Washington Publication 557. Washington, D. C. 1945.

<sup>10</sup>*Physical Chemistry of Cells and Tissues*. By Rudolf Höber, University of Pennsylvania School of Medicine, Philadelphia, Pa., with the collaboration of David I. Hitchcock, Yale University School of Medicine, Laboratory of Physiology, New Haven, Conn.; J. B. Bateman, Mayo Clinic, Rochester, Minn.; David R. Goddard, University of Rochester, Biological Laboratories, Rochester, N. Y.; Wallace O. Fenn, University of Rochester, School of Medicine and Dentistry, Rochester, N. Y. 676 pages. The Blakiston Co., Philadelphia. 1945.

The fourth edition of this **Textbook on Pediatrics**<sup>17</sup> is a successor to the former Griffith and Mitchell edition. Forty-nine authors have contributed the text, edited by Waldo E. Nelson, to meet the needs of undergraduate medical students, as well as both pediatricians and general practitioners. The familiarity of the editor with the previous editions has aided him in giving an excellent sense of unity to the many contributions.

There is much of interest and value in this book for the obstetrician who is concerned with the problems of the newborn infant and the premature infant, as well in the discussions on congenital malformations and diseases, the thymus gland, and erythroblastosis. Those who must combine pediatric practice with obstetric work will find the present text a useful reference work.

PHILIP F. WILLIAMS.

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<sup>17</sup>**Mitchell-Nelson Textbook of Pediatrics.** Edited by Waldo E. Nelson, Professor of Pediatrics, Temple University School of Medicine. 1,329 pages. 519 illustrations, 26 color plates. Fourth edition, revised. W. B. Saunders Company, Philadelphia and London. 1945.

**Synopsis of Physiology** by Main<sup>13</sup> is offered as a text for review purposes. While it covers an enormous field, it makes no pretention to hit more than the high spots. In order to accomplish this, the author has confined himself to data applicable only to the human race. He has cut out all debatable material and confesses that the book is dogmatic. Brief mention of some physiological disturbances in disease, however, is included.

Enormous range and the compactness of the synopsis makes detailed review quite impossible. However, it may be said that for anyone acquainted with the basic facts of physiology this text is of utmost value for review purposes or refresher. The information is accurate and detailed, well up to date.

R. T. FRANK.

**Cornell Conferences on Therapy (Volume I)**<sup>14</sup> is a forum in which pharmacologic and practical therapeutic problems are discussed informally. The fifteen contributions have appeared either in the *Journal of the American Medical Association* or in the *New York State Journal of Medicine* between 1942 and 1945. Very pertinent and practical questions are discussed, such as the "use and abuse of bed rest"; "treatment of heart failure"; "management of abdominal distention"; "the Rh factor in therapy." The book is well worth attention.

R. T. FRANK.

The author, in this short monograph,<sup>15</sup> presents a concise epitome of what is the present concept of essential hypertension. He has gathered the extensive and widely scattered literature, weeded out the nonessential, and gives the important facts only.

He emphasizes the fact that the disease affects the whole vascular system, that the characteristic lesion is a diffuse hyperplastic sclerosis of the arterioles. Clinically, the majority of cases are slow but progressive, the malignant variety being uncommon. The various modes of therapy are described. The monograph is well put together and well illustrated.

R. T. FRANK.

This new book, **Preventive Medicine and Public Health**,<sup>16</sup> is offered to introduce medical students to a new point of view in medical education; that the physician in practice in a community has a responsibility of preventing illness not only among his own patients but in the community. The author regards preventive medicine as an essential part of a physician's clinical practice. He briefly discusses environmental sanitation, gives a more extended discussion of communicable diseases, which is community public health, then proceeds to the subject of child hygiene and adult health protection and promotion. In these chapters there are excellent discussions of the development of child health protection, including maternal care, and such individual problems as mental hygiene, cancer, hypertension, and allergies. In the section on public health administration there are two chapters which merit attention; "adequacy of medical care," and a "national medical care program." The author is not at all biased in his analysis of the various studies that have been made, and he feels that medical care programs should be developed locally, according to the needs of each community, and spread upward rather than being directed from a central source.

PHILIP F. WILLIAMS.

<sup>13</sup>**Synopsis of Physiology.** By Rolland J. Main, Ph.D., Professor of Physiology, Medical College of Virginia, Richmond. Illustrated. 341 pages. The C. V. Mosby Company, St. Louis. 1946.

<sup>14</sup>**Cornell Conferences on Therapy. Volume One.** Edited by Harry Gold, M.D., Managing Editor; David P. Barr, M.D.; Eugene F. DuBois, M.D.; McKen Cattell, M.D.; Charles H. Wheeler, M.D. 322 pages. The Macmillan Company, New York. 1946.

<sup>15</sup>**An Introduction to Essential Hypertension.** By Richard F. Herndon, M.D., F.A.C.P. 88 pages. Charles C Thomas, Springfield, Illinois. 1946.

<sup>16</sup>**Preventive Medicine and Public Health.** By Wilson G. Smilie, Professor of Public Health and Preventive Medicine, Cornell University Medical College. 584 pages, illustrated. The Macmillan Company, New York. 1946.

cyst extirpated. Postoperative removal of more fluid from the thorax was necessary but the patient made an otherwise uneventful recovery, and remained entirely well.

The literature is reviewed and differential diagnosis discussed. A registry for the tabulation of cases of Meigs' syndrome is suggested irrespective of the type of ovarian tumor found so that a true basis for its incidence may be established.

### Pregnancy, Complications, Etc.

**Finn, William F., and Lord, Jere W.:** Carcinoma of the Colon Producing Acute Intestinal Obstruction During Pregnancy, *Surg., Gynec. & Obst.* 80: 545, 1945.

The case history of a patient, six months pregnant, with carcinoma of the sigmoid and acute intestinal obstruction is reported. A transverse colostomy with decompression was first performed, and two weeks later the tumor was removed, the continuity of the bowel being restored by end-to-end anastomosis. Two weeks after this, the colostomy was closed. The patient was delivered normally at term of a normal infant. The case is reported because of the rarity of this complication of pregnancy with survival of the mother. The good result was, in the opinion of the authors, due to the fact that the carcinoma was operable and that it first manifested itself by the presence of obstruction rather than dystocia or peritonitis.

LT. L. M. HELLMAN, M.C., USNR.

**Schwarcz, Ricardo, and Pinto, Roberto M.:** Prolonged Pregnancy, *Bol. Soc. de obst. y ginec. de Buenos Aires* 23: 337, 1944.

Accepting Wahl's concept that pregnancies which exceed 282.5 days counted from the first day of the last menstruation are prolonged, the authors have observed thirty-eight of these cases in the past few years. The pregnancies ranged from 290 to 315 days; eighteen were under 300 days, and fifteen beyond this limit, and 80 per cent of the women were primiparas.

From a practical point of view, prolonged pregnancy nearly always occurs with an overdeveloped fetus which may result in serious mechanical dystocias causing fetomaternal morbidity and mortality, or intrauterine death of the fetus probably due to placental changes.

The interventions performed in the reported cases included six applications of forceps, six cesarean sections, one suture of the cervix and the lower uterine segment, and fifteen episiotomies.

All the forceps applications were indicated by dystocia due to excessive fetal size; the weights of the fetuses ranged from 3,520 to 4,500 grams.

No fetal or maternal mortality resulted from any of the interventions. However, there were four intrauterine fetal deaths, two of which occurred during the last days of pregnancy and two at the beginning of labor which was medically induced in one case. The duration of the four pregnancies was 290, 305, 310, and 315 days, respectively. Of the four dead fetuses, three were males; the preponderance of this sex in prolonged pregnancy has been observed by other authors.

The excessive size of the fetus and its possible intrauterine death are the two fundamental factors on which are based the rules which obtain for the treatment of prolonged pregnancy. When the pregnancy reaches 280 days, careful observation of the woman is started, and this period is extended for twelve days. Between 292 and 302 days is the period of alarm when the various methods of interruption of pregnancy are considered; two methods are preferable: medical induction and cesarean section.

Primary cesarean section is indicated in cases of fetal suffering, excessive fetal size (pelvicofetal disproportion) and previous fetal death in prolonged pregnancy.

J. P. GREENHILL.

# Selected Abstracts

## Gynecology

Di Guglielmo, Lorenzo, and Pepe, Antonio L.: Tuberculosis of the Endometrium, *An. d. Inst. matern. y asist. social, Buenos Aires* 5: 168, 1943.

The authors report a case in which the diagnosis was made by histologic examination of the material obtained through exploratory curettage.

The patient, aged 22 years, had dysmenorrhea beginning with the first menstruation at the age of 13 years. She married at 15 years of age, had never conceived, and had had amenorrhea since the age of 17 years, for which she was treated with estrogens to no avail. She had genital hypoplasia and 40 per cent lymphocytes in the blood.

This case is instructive in that it indicates that in adolescent females with dysmenorrhea or amenorrhea present since puberty, before making the diagnosis of an endocrine disorder and prescribing hormonal therapy, as was done in this case, a specific infection should be ruled out, a point that many specialists are apt to forget.

J. P. GREENHILL.

DeCarle, Donald W.: So-Called Endometrioma Interstitiale, With the Report of Three Possible Cases, *West. J. Surg.* 53: 48, 1945.

Interstitial endometrioma is a disease in which the interstitial cells of the endometrium take on the property of invasive growth. Under hormonal stimulation (estrin) these interstitial cells may invade the myometrium. In the chronic type the cells may stimulate fibrous tissue structure. If localized growth occurs, it may resemble a cellular fibroid. Until Goodall's original description of these tumors, they were all classified as sarcoma of the uterus.

Two types of growth can occur: a generalized increasing of uterine mass, which on the cut section is pinkish-gray in color; or there may be local tumor formation, which on cut section appears as small yellow patches through the myometrium. The author reports three cases. In all of them, there was enlargement of the uterus, and, at the time of the operation, all were suspected of having sarcoma. Microscopic section from the myometrium of these uteri showed numerous strands and islands of tissue resembling endometrial stroma. Occasional mitotic figures were seen. Overgrowth of muscle and fibrous tissue is associated with this pathologic state.

This condition is a benign one, secondary to overstimulation by estrin. It is important that these cases be differentiated pathologically from sarcoma of the uterus.

WILLIAM BICKERS.

Millet, J., and Shell, J.: Meigs' Syndrome in a Case of Multilocular Pseudomucinous Cystadenoma of the Ovary, *Am. J. M. Sc.* 209: 327, 1945.

In this careful case report the authors call attention to the importance of recognizing Meigs' syndrome, which, when correctly diagnosed and properly treated, results in 100 per cent cure. The undiagnosed cases may end fatally.

The case reported is the second on record involving the combination of pseudomucinous cystadenoma accompanied by ascites and hydrothorax. It occurred in a 39-year-old woman whose complaints were referred primarily to the chest. After x-ray examination the chest fluid was removed by repeated thoracentesis, and at operation a large ovarian



a derangement during pregnancy of a dynamic equilibrium between placental acetylcholine on the one hand, and "a set of endocrine factors which conduce to intrinsic hypertonicity and augmented reactivity to vasopressin of the arterioles, i.e., overactivity of the endocrine glands," on the other. Dislocation of this equilibrium in toxemia is reflected in the low acetylcholine content of the placenta and the resulting inadequately opposed action of naturally selected vasopressin.

FRANK SPIELMAN.

### Puerperium

De la Colina, Carlos E., and Dixon, Juan: Pyosalpinx Evacuated Spontaneously Through the Uterine Ostium of the Tube, *An. d. Inst. matern. y asist. social*, Buenos Aires 5: 31, 1943.

The authors report a case of a puerpera in whom spontaneous evacuation of a left pyosalpinx occurred through the uterine cavity. This phenomenon was followed by complete regression of the inflammatory process, which makes the authors believe that the evacuation of pus must have taken place through the uterine end of the tube. Total absence of symptoms in contrast to what would have occurred had the abscess ruptured through a different route lends support to this assumption.

J. P. GREENHILL.

Gavioli, Ricardo L.: Antigalactogens, *Bol. Soc. de obst. y ginec. de Buenos Aires* 23: 348, 1944.

The author states that, although the ideal result has not yet been reached after several years' experimentation with various products to combat engorgement of the breasts and its symptomatology, an acceptable average has been obtained in the suppression or frank diminution of the syndrome to the point that nowadays it is rare to find in the maternities a patient who is incapacitated for several days by lancinating pains in the breasts.

The use of any antigalactogenic substance (camphor, testosterone, estrogen, stilbestrol) even in high dosage has never caused any important disturbance attributable to the substance.

Gavioli has availed himself of this action of stilbestrol on various occasions to stop the production of milk at the time of weaning, using doses varying from 10 to 30 mg. injected in three or more days. He feels justified in drawing the following conclusions.

The most active antigalactogens are the estrogens, particularly the synthetic ones. Their use presents no inconveniences.

Injection of a single dose of 10 mg. of stilbestrol within twenty-four hours after delivery has given successful results in 92 per cent of the cases. If treatment is started late when the engorgement is beginning or already present, the first dose of 10 mg. must be followed by a similar dose after twenty-four hours if the result is unsatisfactory.

Natural estrogens occupy second rank as antigalactogen and is also used in high doses of from 50,000 to 100,000 units in one or two injections during the first hours of the puerperium.

J. P. GREENHILL.

### Cancer, Malignancies

Sandler, Bernard: Principles of Treatment of Carcinoma Cervix Uteri by Radiotherapy, *Proc. Roy. Soc. Med.* 38: 175, 1945.

A great deal of tumor response to radiation depends upon the biologic behavior of the tumor cells. The author feels that cytologic research is especially needed for study of carcinoma of the cervix. High single dosage of irradiation may be an unnecessary, uneconomical, and even harmful process because the same dosage may produce damage to normal cells. The physical problems of dosage are important. In the uterus variations of

Leon, Juan: *Maternal Mortality in the Province of Buenos Aires*, *Bol. Soc. de obst. y ginec. de Buenos Aires* 23: 198, 1944.

The author found that in 1,040,271 assisted labors from 1929 to 1943, inclusive, there were 2,513 maternal deaths (2.38 per thousand) which is a low average mortality. The mortality has decreased notably during the last five years and especially since 1940.

This figure far from correctly reflects the reality, as is the case with all figures taken from public records in most countries; therefore, the Directors of Statistics and Civil Registry and the General Director of Hygiene have imposed recently a number of rules to insure the accuracy of the data in the future.

There are undoubtedly various factors which favorably influence the maternal mortality in the Province; greater resistance of rural women, smaller number of aged primiparas, lower frequency of interventions, and especially transfer of serious cases to the Federal Capital.

Generalized septic processes not due to abortive maneuvers are the principal causes of death (0.14 per cent); however, a decrease in puerperal septicemia and pyemia has been noted during the last few years. Next in importance are hemorrhages of varying nature, occurring during pregnancy, labor, and the puerperium; these accidents have also decreased with time.

Deaths due to abortion represent only 8.6 per cent of the total maternal mortality; this is remarkable in view of the widespread practice of abortion in the Province.

The accidents of labor, which used to be frequent in the rural regions, caused only 117 deaths.

J. P. GREENHILL.

Kunz, A. C., and Raffo, J. C.: *The Future Renal Function of Eclamptic Patients*, *Obst. y ginec. latino-am.* 2: 683, 1944.

A series of twenty-three eclamptic and ten pre-eclamptic patients was followed up by the authors from one to five years after their illness. Chronic nephritis and hypertension were found in 82.6 per cent and 26 per cent respectively of the women who had had eclampsia, and in 70 per cent and 20 per cent respectively of the pre-eclampsia group. Clinical symptoms of chronic nephritis were present in all but two women. These symptoms disappeared after a low nitrogen and low salt diet. The authors emphasize the necessity for prolonged control of women who have had eclampsia or pre-eclampsia.

J. P. GREENHILL.

Hofbauer, J.: *Endocrine Factors in the Mechanism of Toxemia of Pregnancy*, *Am. J. Surg.* 65: 361, 1944.

In presenting his theory regarding the causation of late toxemia of pregnancy, the author states that efforts aimed at the isolation from the placenta of toxins capable of reproducing hypertension and characteristic lesions in vital organs of laboratory animals are "disillusioning exercises." He also regards attempts at assigning an etiological role to the variations in the high chorionic gonadotropin and estrogen titers in the blood as not being acceptably proved. The placenta is thus ruled out as the cardinal factor in the etiology of hypertensive toxemia. Reviewing investigations that go back to 1918, the theory is advanced that toxemia represents disordered autonomic physiology as the result of an undue posterior pituitary (pitressin) effect. The work of numerous authors is cited to support this idea, including the similarity of blood chemistry in eclampsia and in experimental hyperpituitarism, the consistently present "melanophore expanding principle" in the blood of the toxemic patient, the reproduction of the lesions of eclampsia in animals by the administration of proteids followed by pituitrin, the production of permanent hypertension in rats by intraperitoneal and intrathecal injections of pitressin, and the importance of pitressin in the origin of lesions in the liver and kidney in eclampsia through the medium of vascular spasm and anoxia. Of particular importance is recent work describing

# Items

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## American Board of Obstetrics and Gynecology, Inc.

### Examinations

The next written examination (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 7, 1947, at 2:00 P.M. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year. All applications must be in the office of the Secretary by Nov. 1, 1946. Candidates in military service are requested to keep the Secretary's Office closely informed of changes in address.

A number of changes in Board regulations and requirements were put into effect at the last annual meeting of the Board held in Chicago, Illinois, from May 5 to May 11, 1946. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. At this meeting the Board also ruled that it will not accept the nine months' residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration, April 1, 1946.

Applications are now being received for the 1947 examinations. Final examinations will be held in Pittsburgh, Pa., June 1 to 7, 1947. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

PAUL TITUS, M.D.

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The following diplomates have been certified and are added to the previously published list: Dr. Herbert Malone Black, 1517 Hampton Avenue, Walterboro, South Carolina; Dr. Emerson Kenney Blewett, 500 W. 33rd Street, Austin, Texas; Dr. Clair Beebe Crampton, 119 Main Street, Middletown, Connecticut; Captain Willard G. French, M.C., A.U.S., Fort Monmouth Regional Hospital, Ft. Monmouth, New Jersey; Dr. Stanley J. Goodman, 118 Sherman Place, Jersey City, New Jersey; Dr. Thomas G. Gready, Jr., 1314 25th Street, Galveston, Texas; Dr. Eugene Green Hamilton, Suite 320 Lister Building, 4500 Olive Street, St. Louis, Missouri; Dr. Seymour Milton Katz, 170 East 77th Street, New York, New York; Dr. Leon S. Loizeaux, Jr., 4 East 88th Street, New York, New York; Dr. Charles McL. Mulherin, 1211 Greene Street, Augusta, Georgia; Lieutenant Lester D. Odell, M.C., USNR, Naval Air Station, Pensacola, Florida; Dr. Alfred Jacob Platt, 5410 N. Winthrop Street, Chicago, Illinois; Dr. William Raymond Richards, AAF Station Hospital, Greenville Army Air Base, Greenville, South Carolina; Dr. William Robert Schumann, 1338 Gates Place, South Pasadena, California; Dr. Ernest Meyer Soloman, 58 E. Washington Street, Chicago, Illinois; Dr. John Aloysius Sullivan, 764 Queen Ann Road, Teaneck, New Jersey; Dr. Frederick Wendell Temblyn, 803 American State Bank Building, Lansing, Michigan; Dr. William Francis Thomas, Jr., 354 N. Highland Street, Fayetteville, Arkansas; Major Leslie Howard Van Raalte, M.C., Station Hospital, 354th AAF Base Unit, Rapid City Army Air Field, South Dakota.

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### Erratum

In the August issue of the JOURNAL (52: 311, 1946) Leon C. Chesley, Ph.D., S. A. Cosgrove, M.D., F.A.C.S., and John Preece, M.D. wrote an article on hydatidiform mole in which several of the references appeared in error. The corrected references are:

- 9. van Deurs: *Neue Ztschr. f. Geburtsh.* 13: 456, 1843.
- 16. Haase: *Neue Ztschr. f. Geburtsh.* 11: 257, 1841.
- 21. Krieger: *Monatschr. f. Geburtsh. u. Frauenkrank.* 24: 241, 1864.
- 34. Steinberger: *Neue Ztschr. f. Geburtsh.* 2: 96, 1834.

length, the presence of fibroids, distortion by the carcinoma itself, lateral deviation, acute anteversion, or retroversion will affect the dose delivered. In the vagina the variations depend upon the size, shape, and distensibility of the vaginal vault. Alterations in the relative positions of the organs in the pelvis during and after treatment are frequent. Each size of vagina must have its own variation in technique.

X-ray therapy must reach those sites not adequately treated by the radium. The pelvic wall seems to be the most important. If x-ray is to be used after radium, the amount of x-ray to be used depends upon the amount of radiation delivered by the radium. The author's scheme of treatment is as follows:

1. Palpation, colposcopy, cystoscopy, proctoscopy, and pyelography should be routine to ascertain the limits of the primary tumor and its spread.
2. Plan of x-ray, radium, and surgical therapy.
3. X-ray of position of radium.
4. Variation in the position of the radium during treatment must be investigated, and the dose distribution analyzed.
5. Serial biopsies for cytological analysis and guidance for dosage should be undertaken in cooperation with a cytologist.

WILLIAM BERMAN.

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## Necrology

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GEORGE HOPE RYDER, A.B., M.D., of New York City, Clinical Professor of Obstetrics at the Sloane Hospital for Women from 1907 to 1937, a graduate of Yale in 1894, and the College of Physicians and Surgeons in 1899, co-author with the late Dr. Edwin B. Cragin of the *Practice of Obstetrics*, Consultant in several New York Hospitals, Fellow of the American College of Surgeons, Diplomate of the American Board of Obstetrics and Gynecology, died at his home in Babylon, Long Island, on August 27, after a brief illness, at the age of 73 years.

and Private Services at the Jefferson Medical College Hospital between Sept. 1, 1921, and Sept. 1, 1942, formed the basis of that report. Of these patients, 75 were eligible for the consideration of a five-year survival rate, based on various methods of treatment, and irrespective of the stage of the disease encountered.

The former reviews dealt rather exhaustively with basic findings relative to age incidence, parity, menopausal relationships, duration of symptoms, diagnosis, and associated pathology—findings largely in accord with those of other observers. Most of the data presented in our more recent report substantiated those previously presented, and a further summary along these lines of investigation would be an unnecessary repetition. Of greater interest, we believe, is a summary of our present end-results, in comparison with changing concepts of management and treatment, especially in the light of the controversial factors that do exist.

Both of the earlier communications terminated with an over-all picture of the end-results of therapy; first, irrespective of the type of treatment; second, with regard to surgery, irradiation, and surgery combined with irradiation, respectively. In addition, patients have been included whose primary treatment was initiated elsewhere. Expressed in percentages, the various results presented were certainly mediocre. Based as they were on the earliest types of management, the final statistics offered did not truly represent the slow, but certain, improvement that was noted clinically as time went on, seemingly because of a more thoroughly planned technique. The time necessary to prove the value of newer concepts of management seems to pass too slowly in terms of improved survival figures, and too rapidly in terms of energy and physical effort expended. One's span of life is pathetically short when there is so much to be learned, so much to be accomplished. Some of our colleagues have criticized us for not being more selective in the presentation of results achieved; why go back, they say, to the dark ages, as it were, in computing present-day results? Perhaps they are right, but our answer has been that sufficient time must elapse before one can be sure that the path so painstakingly followed is really the right one, even though the trends observed have apparently pointed in that direction.

Influenced by these thoughts, we have decided in this presentation not to stress entirely the over-all end-results observed throughout these twenty-four years, but to select for your consideration a more rational approach to the solution of the cure or arrest of fundal carcinoma by selective discussion of the trial and error methods that have finally led to a more or less standardized plan of treatment. In this way we can perhaps interpret our end-results to much better advantage.

Since Sept. 1, 1942, and up to Sept. 1, 1945, 32 additional patients have been observed. The present survey thus provides a consecutive series of 159

TABLE I. PATIENTS OBSERVED AND FOLLOW-UP

YEARS	SEEN	TREATED	FOLLOW-UP PER CENT
1921-42	127	126	100
1942-45	32	31	100
Total	159	157	100
104 Patients eligible for five-year survival statistics			

# American Journal of Obstetrics and Gynecology

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## Original Communications

### CONTROVERSIAL FACTORS IN THE MANAGEMENT OF FUNDAL CARCINOMA\*

LEWIS C. SCHEFFEY, M.D., Sc.D. (HON.), WILLIAM J. THUDIUM, M.D.,  
DAVID M. FARELL, M.D., AND GEORGE A. HAHN, M.D., PHILADELPHIA, PA.

*(From the Department of Obstetrics and Gynecology, Division of Gynecology, and the  
Tumor Clinic, Jefferson Medical College Hospital)*

THERE has been a relatively slow but gradual evolution in the management of fundal carcinoma throughout recent years. While surgery has, and continues to play the major role in treatment, the question at issue today is to what extent irradiation therapy can be relied upon as a valuable adjunct. This is in contradistinction to the thoughts of most of us with regard to the prime importance of irradiation treatment in cervical carcinoma. It is only by careful scrutiny of one's own work and methods, and pooling the same with the experiences of others, that we may perhaps arrive at an honest, if not an indisputable, answer to this query.

It may be stated at the outset that we are strong advocates of the advantages of irradiation therapy in conjunction with surgery as a planned procedure in treating fundal carcinoma. It would seem better, however, first to trace the steps that have led us to this conclusion before presenting the evidence that is so much in agreement with the work of other observers, and finally to outline our present procedure and results.

Our first report relating to the experience of myself and my associates was published in 1937. In 1940 the senior author had the privilege of discussing Norman Miller's complete and convincing paper on the same subject, at which time we both agreed that irradiation prior to surgery was the procedure of choice, although we differed in the technique, Miller preferring x-ray and we, radium. Our second report, published in 1943, represented a continuation of our efforts along the same line. A study of 127 patients, observed on the Gynecologic Ward

\*Read at a meeting of the Obstetrical Society of Philadelphia, March 7, 1946.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

TABLE III. FIVE-YEAR RESULTS WITH INADEQUATE SURGERY ALONE

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940	4	0	0.0
One primary mortality			25.0
1940 to 1945	1	0	0.0
Total primary mortality (Uterus not removed in two cases)			20.0

Recurrent carcinomatosis caused death within five years. Vaginal hysterectomy without adnexal removal was followed by recurrence in less than a year in a second case. A third patient, aged 47 years, operated upon for myoma by the supravaginal technique without preliminary curettage, was found to have adenocarcinoma when the removed fundus was inspected. The cervical stump was cauterized and both adnexa removed, but peritonitis claimed the patient on the seventh postoperative day. In the case of the remaining two patients, exploratory incisions revealed generalized abdominal carcinomatosis.

The first three patients mentioned above were all operated upon fifteen years ago or longer, and in retrospect represent errors in judgment, modified in one instance by technical difficulty. Follow-up x-ray was suggested in the latter case, however, but refused.

We are ashamed of the primary mortality rate recorded in these two tables, even though one of the deaths may be excused on the basis of the patient's substandard physical condition. Present-day intravenous methods and chemotherapy might have saved the other, for whose death we believe our error in judgment was responsible.

### Radium Therapy Alone

During nearly every year covered by this report, one or more patients have been treated solely with intracavitary applications of radium. In a very few instances, there have been repetitions of such applications. With few exceptions, the patients were elderly, either approaching or within the sixth decade of life, and some of them were obviously very poor risks as well. Furthermore, as previously mentioned, subsequent surgery was not clearly visualized as a planned procedure prior to 1928, or thereabouts. Consequently, dependence was usually placed upon the radium therapy alone. Where advanced involvement was suspected, or where subsequent surgery was contraindicated, external irradiation with x-ray complemented the radium treatment. Since 1928, however, we have had to contend with the refusal of some patients to submit to postirradiation surgery. While satisfactory results to date have been experienced in numerous instances, we wonder, in looking backward, whether more patients in our irradiation series might not be alive today had subsequent surgery been carried out. Some individual recurrences, at a date relatively remote from the initial radium treatment, convince us that an opportunity for permanent arrest of the disease has probably been missed in certain instances. Nevertheless, it cannot be denied that patients with diabetes and cardiovascular disease, especially in the upper age brackets, may have lived longer and with less risk than if surgery had been undertaken following the irradiation.

We also believe that it has been the experience of many of us, that a goodly number of patients with fundal carcinoma are so obese as to discourage surgery. Half a dozen such instances stand out in our memory; women in the neighborhood of 250 pounds or more, whom we have lacked the courage, but not the judgment, to operate upon, relying on irradiation for no other reason, and in spite of the fact that they were not in too old an age group. In such circum-

patients, of whom 104 are eligible for a five-year survival study based upon various plans of treatment. No patients are untraced (Table I).

### The Role of Surgery Without Irradiation

Surgery alone, without any form of irradiation, has played a negligible role in the treatment of fundal carcinoma at Jefferson Hospital. Prior to 1928, a few patients were subjected to panhysterectomy with adnexal removal, but since then this has been only an occasional procedure, and for very definite reasons in each case. In previous reports we gauged the end-results obtained with surgery, without regard to its adequacy in all cases. That this was misleading is shown in this report where we have definitely divided the patients treated surgically into the proper categories as noted in the accompanying tables.

TABLE II. FIVE-YEAR RESULTS WITH ADEQUATE SURGERY ALONE

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940	8	5	62.5
One primary mortality (12 days postoperatively)			12.5
1940 to 1945	5	5	(2 to 4 years)
	No primary mortality		
Total primary mortality			7.6

Table II shows a five-year survival rate of 62.5 per cent—eight to twenty years after operation. The postoperative death occurred in a diabetic patient with cardiovascular disease twelve days after operation. All but one of these five patients were operated upon prior to 1930, and primarily because the diagnosis was definitely established or strongly suspected. The remaining patient had a huge myoma, and although endometrial cancer was a definite possibility, diagnostic curettage demonstrated that the uterine cavity was unsuitable for a preliminary radium application, and radical operation was proceeded with at once, six years ago.

Three of the five patients operated upon within the past five years had been treated with radium for benign conditions four to eleven years previously, and are part of a group of patients reported upon several years ago at a meeting of the American Gynecological Society. In a sense, one could say that irradiation might have been responsible to some extent for their present-day survival, but such a conclusion is purely presumptive. The remaining two patients were operated upon for myoma and ovarian cyst, respectively, and radical operations were performed routinely in the first case and because of a frozen section diagnosis of ovarian carcinoma in the second case (metastatic from uterus).

We do not know why follow-up x-ray was not used in the case of the two patients adequately operated upon in 1923, but who lived less than a year thereafter. We do know, however, that x-ray was not employed as a follow-up measure in the 10 patients surviving from two to twenty years, because it was believed that the surgery was sufficiently complete and because there was no visual or palpable evidence of pelvic or abdominal extension beyond the removed uterus and adnexa. We will comment again with reference to our failure to use routine postoperative x-ray when the surgery seems to be complete and adequate.

Table III groups the patients having inadequate procedures, only one of whom survived longer than a year. In 1926, a positive diagnosis was made in one patient by curettage when a polyp was removed; a radical operation was planned, but not consummated because a fairly large adherent ovarian cyst interfered technically. The remaining cervical stump was cauterized from above.



TABLE V. FIVE-YEAR RESULTS WITH X-RAY ALONE

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940	1	0	0.0
1940 to 1945	1	0	0.0

Primary treatment elsewhere in one case)

TABLE VI. FIVE-YEAR RESULTS WITH RADIUM AND X-RAY

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940	30	11	36.6
(4 additional patients survived 6 to 8 years, but died of cancer)			
1940 to 1945	7	3	(1 to 2 years)

No primary mortality  
(Primary treatment elsewhere in one case)

per cent—were between 55 and 75 years of age, and regarded as doubtful surgical risks from several angles.

Table V shows that only two patients were treated with x-ray therapy alone—exceedingly advanced cases.

Table VI shows that 37 patients have been so treated, of whom 30 are eligible for five-year statistics—the survival rate being 36.6 per cent, definitely lower than in the similar numerical group receiving radium alone. This might be expected because the lesions observed were relatively farther advanced.

Three patients in this group are deserving of special mention. Two of them, aged 37 and 40 years respectively when treated primarily ten to thirteen years ago, exhibited high-grade malignancy in the eutettage, and both refused subsequent surgery. Repeated eutettage at intervals since has been negative. This is also true of the third patient, aged 40 years and excessively obese, but exhibiting a low-grade lesion primarily. We hesitated to operate upon this patient.

The factors employed in our x-ray therapy are 25 Ma. at 200 kv., filtered through 0.5 mm. or 1.0 mm. of copper and 1.0 mm. of aluminum at 50 cm. S.T.D.; ports 16, 19, or 20 cm. square. Two anteriorly and two posteriorly are employed at first, cross-firing the uterus and parametrium. Two such areas are treated daily, each receiving 200 r. (measured in air). The treatments are continued until a well-marked erythema is obtained, which in general will occur with a total of 1,600 to 2,400 r. to each portal. Three to four weeks are required to complete the cycle, but if the time is not restricted, and to avoid sickness, the daily r. treatment is reduced, and the treatments extended over a longer period of time.

### Experiences With Surgery and Irradiation Combined

Irradiation therapy in some form as an adjunct to surgery furnishes an interesting analysis with regard to results. In previous reports, patients were included indiscriminately in this grouping, even when the surgery was limited to an exploratory laparotomy. Such an inclusion may be quite correct in computing an absolute survival rate, but it is of no value in estimating the worth of a particular type of treatment. It seems much fairer to consider separately the character of the surgical procedure together with the circumstances that determined it, and the manner in which the associated irradiation was utilized. Accordingly, we have chosen to break down the entire group of 69 patients so treated into three categories: first, those in whom the surgery was inadequate or incomplete and accompanied with some form of irradiation in addition; second, those in whom the surgery was adequate and essentially complete, with irradiation

stances we believe that it is advisable to repeat curettage and radium at selected intervals, even in the absence of recurrent bleeding. This procedure seems to have justified itself in the present-day survival rate noted in certain of these individuals.

It has been interesting to break down the irradiation group for specific analysis, for it is evident that there will always be certain patients in whom irradiation therapy will have to be relied upon for the reasons mentioned. It is commendable to be an idealist, but one cannot always practice idealism, at least in surgery.

TABLE IV. FIVE-YEAR RESULTS WITH RADIUM ALONE

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940 (2 additional patients; surviving six and seven years, still have cancer; another survived six years, but died of cancer)	24	11	45.8
1940 to 1945	7	6	(2 to 4 years)
No primary mortality			

Table IV shows that 31 patients have been treated solely with radium, 80 per cent of whom have ranged in age from 55 to 77 years. Of 24 eligible for five-year statistics, 11 have survived from five to seventeen years—45.8 per cent. The remainder of the table is self-explanatory.

Four patients refused subsequent surgery. One is bed-fast; three are alive from two to seventeen years. Two received radium for benign conditions six and twelve years before receiving treatment for definite endometrial cancer. In the latter case, a review of the original slide showed a diagnostic error. It is astonishing that this patient's malignancy was impotent for so long a time; on the basis of this, and because of her advanced age, it was decided to employ only a large dosage of radium, which she has now survived seven years without signs of recurrence. Two excessively fat women, with low-grade malignancies, have been treated with radium alone (repeated in one instance) and are free of symptoms for two to four years, respectively. Relatively early deaths in 11 patients following radium treatment alone, apparently indicate that more advanced disease was present than was estimated when radium alone was chosen for these individuals. Chiefly over 60 years of age, none of them survived longer than three years.

There was no immediate mortality in this group. The radium dosage during the past decade has averaged 4,500 to 5,000 mg. hr. (screening with 1.5 mm. of platinum). Previously, the dosage varied from 2,400 to 3,600 mg. hr. (0.3 mm. silver and 1.0 mm. brass, or 0.5 mm. platinum-screening prior to 1937). Fewer complications were noted than in cervical carcinoma with radium therapy.

### Radium Therapy With X-ray in Addition

Whenever it is thought that endometrial cancer is deeply invasive or has passed beyond the confines of the uterus, deep x-ray therapy is used to supplement the radium. This is as true of the past as it is of the present. X-ray has been used more frequently after the radium application. Whereas the radium applications were rarely repeated in those patients who were treated with it alone, it has not been uncommon for patients receiving x-ray in addition to have had several intracavitary applications, especially with recurrence of symptoms. This is understandable, for those patients receiving both types of irradiation therapy were more likely to represent advanced cases, or cases too advanced to depend upon radium alone. Here again, the majority of the patients—75

x-ray was ineffectual, death occurring three years later. Incomplete surgery may have been at fault.

In four instances, exploratory operation was all that could be accomplished because of inoperability, and postoperative x-ray was used in all instances, as well as radium in one case. Only one patient survived as long as five years; all died of cancer. These cases were relatively hopeless from the start.

In one patient, radium to the uterus for endometrial cancer was accompanied with laparotomy for metastatic ovarian carcinoma and resection of an independent cancer of the sigmoid. Follow-up x-ray was used, the patient surviving for two and one-half years—practically a hopeless picture from the beginning.

Another patient was given radium to the uterine cavity and x-ray postoperatively, following the removal of bilateral ovarian carcinomas with implants (metastatic), death occurring within two years; a difficult and inoperable case when seen primarily.

In the group of 13 patients eligible for five-year survival statistics, it will thus be seen that the three patients surviving more than five years had their uteri removed supravaginally, there was no evidence of cancer in the retained stump, and postoperative x-ray was employed in addition. Of the remaining 10 patients, hysterectomy was part of an incomplete operation in five instances, the accompanying irradiation was ineffectual, and to all of them, errors of judgment might be charged. In five other cases, the uterus could not be removed because of inoperability when first seen, instances of delayed diagnosis.

Of the four patients treated within the past five years, three are surviving the supravaginal operation with postoperative x-ray, and doing well because the cervix and adnexae were apparently uninvolved. A patient with metastatic cancer in both ovaries was obviously inoperable when first seen.

The importance of preliminary curettage and the necessity of always thinking of endometrial cancer as an accompanying lesion in the presence of myoma in the menopausal and postmenopausal age groups when planning immediate surgery is well demonstrated in the analysis of the patients in this group. The low survival figure is indicative of such errors.

TABLE VIII. FIVE-YEAR RESULTS WITH ADEQUATE SURGERY PLUS RADIUM AND/OR X-RAY (UNPLANNED TECHNIQUE)

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940	16	6	37.5
(One additional patient survived 7 years, but died of cancer)			
1940 to 1945	5	4	(1 to 4 years)
No primary mortality			
(Primary treatment elsewhere in one case)			

II. *Adequate surgery with some form of irradiation in addition (unplanned technique).*—Table VIII shows a five-year survival of 37.5 per cent. There were 16 patients in this group, all of whom had complete hysterectomy with bilateral adnexal removal. Of these, six were operated upon prior to 1930, when the only form of irradiation that we were using in addition to adequate surgery was postoperative x-ray. Only one has survived—for 19 years; four died within one year; one survived three years.

Another group of seven were operated upon after that period, and of these three have survived from five to ten years, one lived for seven years but died of cancer, and three died within a year of operation. All received preliminary radium and x-ray, although one received x-ray elsewhere for a myoma before we correctly diagnosed endometrial cancer. One survivor, and one who died within a year, also received postoperative x-ray.

tion in addition, but not employed according to any set plan; third, that group of patients in whom adequate surgery followed preliminary intrauterine radium applications according to a definitely conceived technique.

I. *Inadequate surgery with some form of irradiation in addition.*—By inadequate surgery we mean anything short of complete hysterectomy with adnexal removal. Table VII, showing only a 23 per cent five-year survival rate, requires some explanatory remarks.

TABLE VII. FIVE-YEAR RESULTS WITH INADEQUATE SURGERY PLUS RADIUM AND/OR X-RAY

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940	13	3	23.0
(3 additional patients survived 5 to 7 years, but died of cancer)			
1940 to 1945	4	3	(2 to 3 years)
No primary mortality (Primary treatment elsewhere in 3 cases) (Uterus not removed in 6 cases)			

Taking all the patients in the table into consideration, we find that supravaginal hysterectomy with adnexal removal was carried out in five patients under our direction. In two of them, endometrial cancer has been diagnosed by preliminary curettage. This was in 1930, before we were applying radium first, and radical operation was immediately planned. This could not be carried out completely because of technical difficulties, but both cervical stumps were cauterized from above and thought to be free of cancer, as shown by histologic study of the removed uteri. Follow-up x-ray was administered, and the patients have survived 11 and 16 years, respectively, without recurrence. In the remaining three patients, cancer was not suspected, and no preliminary curettage was done. Radium was applied to the left broad ligament, followed by x-ray therapy in one instance, and to the cervical stump in another—both patients eventually dying of cancer, although one survived seven years. Both were operated upon twelve to fifteen years ago. The third patient in this group, operated upon two years ago without preliminary curettage, and as a myoma case, had received some x-ray therapy elsewhere before coming to us. She has had postoperative x-ray, and remains well and symptom-free at present. However, the treatment of this patient and the other two represents definite errors of judgment in our primary management of these patients, but with a relatively fortunate outcome.

Supravaginal hysterectomy with adnexal removal was carried out elsewhere in three patients, the operations having been performed for myoma without preliminary curettage or any suspicion of endometrial cancer, the latter being discovered in the removed uteri. Postoperative x-ray has been supervised by us, the patients now surviving three to five years; all errors of judgment primarily but with good result to date, possibly because the amputation was sufficiently low.

Two patients had vaginal hysterectomy without adnexal removal. In one, the operation was for procidentia, the cancer being found by the pathologist in the removed uterus. Postoperative x-ray was effective for a few years only. The other patient, primarily treated twice with intrauterine radium as a bad surgical risk, was persuaded to have a vaginal hysterectomy elsewhere, but without adnexal removal. She survived the operation but died within five years of carcinomatosis. Errors in judgment can be charged in both cases—failure to perform diagnostic curettage in the first instance, accounting for incomplete surgery, and unwise and inadequate surgery in the second case.

One patient with preliminary radium had subsequent panhysterectomy, but one adnexa was allowed to remain—why, we do not know—and follow-up

pausal bleeding. During the past five years, 21 more patients have been treated according to plan, of whom one died suddenly of an embolism two years after treatment. There was no autopsy, but the attending physician said that there was no gross evidence of recurrent cancer. There are six four-year survivors; five have survived from two to three years, and the remaining nine approximately one year, more or less.

Our procedure has been pretty well standardized. Whenever we suspect the possibility of endometrial carcinoma, preparation is made for diagnostic curettage, and radium capsules are available for immediate intrauterine application. If there is no physical contraindication to use of the radium, either 50 or 100 mg. are placed in situ, while the curettings are examined by an especially rapid staining paraffin technique which enables us to get a report in four hours. If malignant, a dosage of 4,500 to 5,000 mg. hr. is administered. If not malignant, dosage suitable to a benign condition is employed. If we consider the patient to be a favorable risk, complete surgery is carried out, preferably in six to eight weeks. We have gradually increased our conception of what constitutes a good surgical risk, and we endeavor to follow through with surgery in every possible instance. If there is visual or palpable evidence of carcinomatous extension, or if recurrence is noted, then follow-up x-ray would have to be relied upon. We do not favor it merely as a routine postoperative measure, because of the unpredictable effect upon the intestinal tract. Thus far, none of the patients in this series have received any. In only one patient was carcinoma definitely found outside the uterus, and that was in an ovary. In another patient, the possibility of a concomitant Brenner tumor of the ovary has been considered.

Except in one case, it was thought clinically that cancer was still confined to the uterus, and this was pretty well borne out by the pathologic reports. In 17 uteri (54.8 per cent) residual carcinoma was found, often attenuated, sometimes infiltrating. Usually, alteration of the architecture of the growth, marked destruction, necrosis, and even ulceration of the endometrium have been reported. This fact alone should be of consolation to us when we have to depend upon irradiation therapy in the patient unsuited to operation for any reason. There was nothing too unusual with regard to the symptomatology. An average delay period of six months or so was frequently noted. The majority of the patients were in the 50's and 60's; only six were under 50 years of age.

Nearly two-thirds of the lesions were classified as low-grade malignancies; the remainder were evenly divided between intermediate and high-grade ones. Three of the latter are among the five-year survivors. No conclusions can as yet be drawn from this information, except to say that, in our experience, low-grade lesions often do very well with radium alone, and certainly do so with surgery. Perhaps that is because there are more of them observed in a relatively large series of patients. Radiosensitivity and radiocurability are not synonymous terms in the belief of most of us.

We feel that radium has a distinct advantage when used preoperatively; not only because it causes local cancer destruction, but because it may devitalize the growth, even at some distance from the radium and without altering its microscopic appearance. This we cannot prove, but it is our impression that if such an action is possible, it may be a factor that tends to discourage local recurrence after surgery. Then, too, we have noticed a general improvement in some patients between the time that the radium was applied and the time of the operation. There was no primary mortality in the preirradiated group, furthermore.

Preoperative x-ray probably acts in the same way. A few years ago, Norman Miller and our group agreed to follow our respective ways with relation to our methods of preoperative irradiation—he used x-ray, and we used radium.

Three remaining patients in this group are worthy of comment. One had received radium elsewhere sometime before our operative treatment of her. This was in 1927, and we were unable to obtain correct information regarding her former treatment. She died of spinal metastases within a year of our operation. The second patient, operated upon in 1928, had an interposition operation together with radium for metropathia hemorrhagica. Routine curettage revealed endometrial cancer, and complete surgery was performed a few months later. The patient survived eight years, developed insanity, and committed suicide. The third patient was treated with radium in 1936 at the age of 61 years, with apparent arrest of symptoms; seven years later she was readmitted because of pyometra, and complete operation was performed at the age of 68 years. Extensive carcinoma was present in the uterus. She has remained well and symptom-free for two years, now aged 70 years, and nine years since her initial treatment.

It was this transition period in our work that convinced us of the efficacy of preoperative irradiation. We were impressed with the destructive action of the radium upon the endometrial carcinoma, as noted in the removed uteri, even though attenuated or viable cells were reported present; also, the absence of recurrence in the vaginal vault. We began to note a longer survival period from the work of this 1930 to 1940 decade. What seemed to discourage us about the postoperative x-ray was its apparent ineffectiveness, while its use in a few instances before surgery seemed to cause considerable skin change that necessitated postponement of subsequent surgery. We determined to rely upon preoperative radium only, whenever possible, and to build up such a series of cases.

Of the five patients noted in Table VIII as having been treated within the past five years, one came to us for vaginal recurrence following complete surgery elsewhere. The irradiation received there was postoperative x-ray which we continued, but death ensued a few months later. Two more patients had complete surgery in our hands because of operation for myoma, with unsuspected endometrial cancer in one case, and metastatic ovarian carcinoma in another; postoperative x-ray was employed as a routine, since there had been no preliminary irradiation. A fourth patient received preoperative x-ray because the initial curettage perforated the uterine cavity and radium was not employed. Complete operation followed in three months. The fifth patient had x-ray elsewhere for "menopausal bleeding" before we made the diagnosis of cancer, administered radium, and then performed complete surgery. They have survived for one, two, and four years, respectively.

TABLE IX. FIVE-YEAR RESULTS WITH PRELIMINARY RADIUM PLUS ADEQUATE SURGERY  
(PLANNED TECHNIQUE)

YEARS	PATIENTS	SURVIVORS	PER CENT
1921 to 1940	10	9	90.0
1940 to 1945	21	20	(1 to 4 years)

No primary mortality  
(Residual carcinoma in 54.8 per cent of removed uteri)

III. *Adequate surgery with preliminary radium (planned technique).*—We have been quite a long time in arriving at the most promising part of this presentation. Table IX deals entirely with those patients in whom we have carried out, under our own supervision, a definitely planned technique whenever possible since 1935. The first patient was so treated, however, in 1932, and she has survived for thirteen years. The remainder are alive from five to seven years, thus making up the 90 per cent survival rate. The one death in this group occurred four years after treatment, and was due to cancer. The initial symptom was a metastatic nodule in the vagina. There had been no postmeno-

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## Discussion

DR. CHARLES A. BEHNEY.—One is impressed with the careful study and treatment which the patients comprising the material in this paper received. The results of treatment have been analyzed with painstaking care and thought.

The seemingly high immediate mortality rate for the surgically treated patients simply demonstrates how misleading conclusions drawn from a small series of patients may be. In fact, the great disadvantage in breaking up material into so many categories is that each group comprises so few cases that unusual conclusions should be viewed critically. I believe that this is why the authors present their material and statistics with a request that they be utilized in connection with reports from other clinics, treating patients in a similar manner, so that eventually a large enough series will be secured to make the statistics thoroughly conclusive.

The group of patients regarded unsuitable for surgical treatment interested me particularly. One cannot have a standard treatment for carcinoma of the fundus any more than for any other disease. Certainly, those hypertensive, cardiac decompensative, terrifically obese, etc., women were given a better chance for survival by treating them radiologically than if they had been subjected to the strain of panhysterectomy. It sometimes seems unfortunate that so much emphasis is placed on the five-year survival rate. If the patient is spared from the discomfort and torment of death from cancer, she represents a victory over that disease, whether she lives two months or twenty years after treatment. We cannot agree that a hypertensive patient treated with radium, who dies three years later from a cerebral hemorrhage, should be classified as a failure.

It is interesting to note that among the cases reported, those who had hysterectomies after preoperative radium irradiation showed residual carcinoma in 54.8 per cent of instances, and that the salvage rate in those cases who were treated radiologically and without surgery was 45 per cent. These two observations check so perfectly that it would seem that radium irradiation alone cannot be expected to destroy completely the carcinoma in the fundus of the uterus in more than 45 per cent of the cases. As has been stated, this in itself is sufficient reason for augmenting preoperative irradiation with radical surgery. There is another indication for supplementing irradiation with total hysterectomy. There have been instances in our experience where the intense effect of the radium on the carcinoma produced such extensive necrosis of the uterine wall that perforations and peritonitis followed. This is particularly true when the disease is extensive and when the tumor is especially radiosensitive. Consequently, it is our practice to perform total hysterectomy, regardless of how well our patients seem to do after irradiation.

The essayists again bring up the question of preoperative radium irradiation versus preoperative high voltage x-ray irradiation. One of the arguments in favor of the former is that the preoperative radium irradiation prevents vaginal recurrences. In the group presented, there was one such vaginal recurrence. Another argument in favor of preoperative radium irradiation is that x-ray irradiation is more likely to be followed by deleterious effects on the gastrointestinal tract. By the same token, radium would be less lethal to extensions into the parametrium or other surrounding structures.

An extensive experience with laparotomies following intensive x-ray irradiation for various reasons leads us to disagree with the frequently heard statement that x-ray irradiation makes later surgery more difficult because it produces adhesions, changes in the abdominal wall which interfere with ease of operation or postoperative healing. If the x-ray therapy is administered properly by means of standardized equipment, employing proper



TeLinde, of Baltimore, uses both—radium before, and x-ray after operation. Kamperman uses radium and x-ray preoperatively in some instances, and post-operative x-ray in all.

All that we can do is to show our results to date. It will take much more time and a continuation of our present methods to tell whether we are on the right road and, furthermore, whether we are going in the right direction. We hope and think that we are, as do a goodly number of us (Healy, Ward, Schmitz, and recently, McLennan).

TABLE X. FIVE-YEAR RESULTS OVER-ALL PICTURE

TREATMENT	PATIENTS	SURVIVORS	PER CENT
Surgery	12	5	41.6
Irradiation	55	22	41.8
Surgery and Irradiation (Unplanned)	27	8	29.6
Radiation and Surgery (Planned)	10	9	90.0
	104	44	42.3
PRIMARY MORTALITY			
87 Patients, Surgery performed		(2)	2.3
79 Patients, Uteri removed		(2)	2.5
74 Patients, Uteri Removed (Jeff.)		(2)	2.7
31 Patients, Uteri removed (planned)			0.0

Table X merely indicates how the over-all picture fails to tell the true story in distinct brackets as far as relative five-year survivals are concerned. There are numerous individual variants that have been mentioned. That is why we came to realize that our report of three years ago was cumbersome and misleading with respect to the advances that we felt sure we were making. The relative five-year survival figures then read as follows: surgery alone, 18.1 per cent; irradiation alone, 40.5 per cent; surgery and irradiation, 38.4 per cent (corrected for uteri actually removed, 42.9 per cent). For all cases, irrespective of treatment, 39.1 per cent. The primary mortality, however, gives a clearer picture when viewed from an over-all position, for which we may be grateful.

### Summary and Conclusions

1. In this report emphasis has been placed upon a comparative study of the results obtained in the treatment of fundal carcinoma based upon a critical analysis of the conditions noted and the type of treatment employed in each of several groups of patients, rather than upon an over-all estimate of the end-results obtained without respect to the status of the individual case and the treatment employed.

2. This analysis has shown that in our experience a planned technique of preliminary irradiation with radium, followed by adequate surgery in eight to ten weeks, has resulted in a five-year survival rate of 90 per cent among a group of 10 patients, with 20 additional patients among a group of 21 now surviving from one to four years, and without operative mortality.

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intrauterine applications. Unless adequate external irradiation is precluded by obesity, we treat the inoperable group by both approaches. Because of the recognized dangers of initial overdosage, the external irradiation is administered with the greatest caution, and the intrauterine irradiation is administered in divided doses. The obesity inoperable group is treated only by repeated intracavitary applications.

Since irradiation, when applied within the limits of safety, fails to destroy corporeal cancer frequently, we must hope to feel our way slowly to a more satisfactory technique, or better still to lift some of the patients from the inoperable to the operable bracket. The range of systemic inoperability has been reduced by modern pre-intra and postoperative management, and a similar reduction in local operability may follow further improvements in the technique of irradiation therapy—both external and intracavitary.

DR. SCHEFFEY (Closing).—Many points have been brought up that I would like to comment upon. Dr. Behney is quite right in mentioning the disadvantage of drawing conclusions from a statistical review of small groups of patients. On the other hand, my purpose was to show the unfairness of presenting only the over-all picture with respect to a five-year survival rate, irrespective of the individual problem each patient presents with regard to the physical factors involved, the stage of the disease, and the type of treatment employed—whether it be impossible, inadequate, or carefully planned under favorable circumstances. We have “broken down” the entire series for the very reason that we do wish to evaluate the mortality and the five-year survival rate in the categories mentioned, and in order to show what we have been able to accomplish in a suitable group of patients when it was possible to carry out a definitely planned procedure for these individuals.

If we know for a certainty that a patient who has survived for five years or more has not died of cancer, we do not hesitate to include her as a five-year survivor for statistical purposes. Conversely, even though a patient has passed the five-year standard, and we know that cancer is still present, we should state that fact clearly. We do not want to fool ourselves or anyone else.

Of course we cannot have a “standard treatment” for every patient with fundal cancer. We have brought that out very clearly in this paper, showing the limitations that exist in certain individual instances. We do say, however, that as our experience has increased, we have increased our indications for postirradiation surgery more and more, and with increasingly beneficial results. Our experience has shown, too, that one should not rest content with an initially good result from irradiation therapy, but carry through with subsequent surgery; otherwise unarrested disease or recurrence will very probably happen in 45 to 50 per cent of the patients treated with irradiation only. When subsequent surgery is impossible or inadvisable, it is our practice to perform a test curettage and apply more radium if indicated, in about six months or a year using external irradiation in addition, following the initial radium application. If bleeding recurs earlier in patients of this sort, repeat the treatment promptly with another curettage, of course. This is the plan that we have followed in our excessively stout women. This answers Dr. Outerbridge’s question.

One must be careful of exceptionally larger doses of radium in relatively small uteri. We had an illustration of this recently in an elderly patient. When she returned for the surgical procedure, the patient told of having had an attack of “intestinal gripe” some time after the radium application. At operation, the small uterus was rather firmly attached to the rectosigmoid which was deviated toward the right side of the pelvis. Thickening of the bowel was present, with evidence of a localized peritonitis. The radium had produced as severe an intestinal reaction as is so often the case with intensive external irradiation for cervical carcinoma.

I grant that our impressions of skin damage as a deterrent to later surgery goes back to the days when we saw more intense reactions from external irradiation. Since then the methods of application have improved tremendously, but in the meantime, having ceased using preliminary x-ray in favor of radium, we have not gone back to it, for we have been anxious to build up a series of cases with radium as the sole preliminary agent, as stated in the paper. We grant that those employing x-ray instead report gratifying results, but we limit

filtration, and sufficient time for the reaction to subside is allowed to intervene before the surgery is practiced, the latter will not be rendered less feasible because of the preliminary irradiation.

In our clinic, we use preoperative x-ray irradiation in certain instances, and in others preoperative radium irradiation, depending upon whether a curettage is necessary to arrive at a definite diagnosis. Many of our patients are seen in the Out-Patient Department, where material is secured from the uterine cavity by means of a suction curette. If the pathologic report demonstrates carcinoma of the fundus, the patient is given preoperative high voltage, external irradiation through four abdominal ports. When, however, it is necessary to perform a curettage in order to make our diagnosis, radium is made available, and we practice a technique similar to that described by the essayists. The radium is inserted at the time of the curettage, and a diagnosis by a quick paraffin method is awaited. If the diagnosis is carcinoma, the radium is allowed to remain as long as necessary to secure the usual carcinoma dose. If, however, the tissue proves to be benign, the radium is removed at the proper time for irradiation for benign bleeding. It is our opinion that there is little to choose between the two methods of preoperative irradiation, and we select the method which is most convenient to the patient and less expensive to the hospital. In carcinoma of the fundus, as in most other forms of cancer, the ultimate outcome depends more on early diagnosis and prompt treatment than on any differences of technique.

DR. FRANKLIN L. PAYNE.—We are indebted to Dr. Scheffey for his reminder that the policies of treatment in fundal carcinoma remain open to critical discussion and to revision. At the University of Pennsylvania Hospital we recognize three avenues of approach to the problem: surgery alone, a combination of surgery and irradiation, and irradiation alone. The controversial factors rotate around the wisdom of surgery alone, the efficiency of intracavitary irradiation versus external irradiation or the value of the two in combination, and the technique of intracavitary irradiation—both as to dosage and distribution.

The ideal management would consist of the accurate microscopic diagnosis of corporeal cancer and its immediate removal by total hysterectomy and bilateral salpingo-oophorectomy. This eliminates the danger of dissemination by the curettage, reduces the time that is required for treatment, and obviates the psychic trauma of readmission for a second operative procedure. Objections to this plan include the great difficulty in making a certain diagnosis immediately and the possible value of preoperative irradiation as a localizing agent. Despite these deterrents, we believe that the early cases should be so treated, provided an unequivocal diagnosis is made and no contraindication to radical surgery obtains.

Since this ideal is realized infrequently, the plurality of fundal carcinomas must be treated by a combination of irradiation and surgery. The proper choice of the method or the time of irradiation still is open to question, as Dr. Scheffey indicated. Study of irradiated specimens and careful follow-up analyses after internal irradiation on one hand and external therapy on the other, as planned by Drs. Scheffey and Norman Miller, should do much to give us the correct answer. Thus far we agree with Dr. Scheffey that in the operative group the advantages of external irradiation, either alone or in combination with intrauterine applications of radium, do not compensate for its disadvantages and we do not use it. Our present policy consists of intracavitary irradiation to be followed four to six weeks later by operation. Dissatisfaction with the intracavitary irradiation, as it has been applied, has arisen from study of our operative specimens. Our experience confirms that of Dr. Scheffey that about 50 per cent of the previously irradiated uteri exhibit residual carcinoma at the time of their removal. The works of Sampson, Crossen, and many others indict the old practice of applying radium in tandem for corporeal cancer. Recently we have adopted the technique described by Crossen for intracavitary irradiation. It appeals because of its apparent satisfactory distribution and its simplicity of application.

While careful radium distribution is important in the operative cases, it is even more so in those instances in which entire dependence must be placed upon radiotherapy—because of either systemic or local considerations. Here two questions arise: the advisability of combined external and intracavitary irradiation, and the wisdom of multiple

## A CLINICAL EVALUATION OF ECTOPIC PREGNANCY\*

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**I**N THIS presentation we propose to evaluate and comment upon the facts which have been accumulated from our experience with ectopic pregnancy. The importance of such a study becomes apparent in the light of Williams and Corbit's recent analysis of 101 fatalities from ectopic pregnancy. These authors state that in the decade 1931 to 1940 every eighteenth puerperal death in Philadelphia, every sixteenth puerperal death in New York City, and every twelfth puerperal death in Chicago was due to ectopic gestation. In Philadelphia from 1931 to 1943 the mortality was 4.6 per cent. Within the last ten years reports on the mortality rate have ranged from 3.2 per cent to 8.3 per cent; Fitzgerald and Brewer, 7.8 per cent (1935); Falk and Rosenbloom, 8.3 per cent (1936); Ware and Winn, 8 per cent (1941); Farrell and Scheffey, 3.2 per cent (1943); and Siegler, 3.9 per cent (1945).

### Incidence

In the Woman's Clinic of the New York Hospital from Sept. 1, 1932, to Jan. 1, 1946, there were 41,365 pregnancies cared for, which include 38,356 full-term and premature deliveries and 3,009 abortions. During this period there were 141 ectopic pregnancies, an incidence of 0.34 per cent, or 1 in 293 pregnancies.

Ectopic gestation was found to occur most frequently in the age group ranging from 25 to 35 years (Table I). The youngest patient in the series was 19 years of age and the oldest 41 years of age. Table I also indicates that over one-fourth of the cases occurred in women beyond 35 years of age. It is significant that in this group late marriage, low fertility, and repeated abortions were factors often encountered in the histories.

### Gravidity Antedating the Present Ectopic Pregnancy

An analysis of Table II reveals that 28.4 per cent of the patients had never before been pregnant, and that 43.3 per cent had never previously been delivered of a viable infant. Furthermore, there were only 10.6 per cent who had borne two or more children. These data reflect the generally accepted fact that low fertility and infertility are commonly associated with ectopic pregnancy.

Repeated ectopic gestation was noted in seven patients, or 4.9 per cent. In only one of these was there a previous history of salpingitis eventually verified by pathologic sections.

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external irradiation to those patients being treated with irradiation alone, or in instances where inadequate surgery has obtained, or where extension beyond the uterus has occurred. Dr. Behney's experience is in accord with Dr. Norman Miller's. Perhaps our future experience and that of some of our colleagues may influence us to change our present method, but we are still desirous of continuing with a plan which shows a five-year survival rate of 90 per cent, together with 20 out of 21 additional patients treated during the past five years being alive and well at the present time—and without any operative mortality. With the exceptions noted, and for the reasons stated, Dr. Behney's management of fundal carcinoma differs little, if any, in principle from ours.

Dr. Payne has brought up a very pertinent question—the efficacy of intracavitary radium applications. We are well aware of Sampson's work of years ago in which he showed the inadequacy of proper action from intrauterine radium capsules when the uterine cavity was irregular or distorted. We have called attention to those cases in which it is impossible to secure a good intracavitary radium application as a preliminary procedure when fundal carcinoma is suspected. In several such instances, when the fundus was especially large and irregular on the outside as well as in the endometrial cavity, because of concomitant myomas, we have resorted to immediate panhysterectomy with adnexal removal, as noted in our paper.

Even before Heymann packed the uterine cavity with multiple, small radium units, Burnham had been doing just that in Baltimore, but he discontinued this technique. We have not employed Crossen's method, or Friedman's either. It seems to have merit, however, and I know that we will await with interest a future report of Dr. Payne's end-results with the method of therapy that he is now carrying out at the University of Pennsylvania Hospital. I am glad that he agrees with us in the principle of the present-day treatment of fundal carcinoma that we have presented, irrespective of the controversial issues that have been mentioned. Truly, every patient must be individualized; only those patients falling into the favorable group that we have described can be managed by a so-called "planned technique."

changes favorable for an ectopic pregnancy. Only four patients admitted that they had been treated for gonorrhea, and an equal number stated that severe pelvic inflammatory disease followed an induced abortion. Among the cases of appendicitis, liberally assuming that all appendectomies were performed for appendicitis, there were as many left as right salpingectomies done for an ensuing ectopic pregnancy. More important is the number of times that the diagnosis of salpingitis was made by microscopic examination when the pathologic anatomy of tubal pregnancy was reviewed in each case. This lesion was unequivocally seen only twenty times, or 14.2 per cent. It is doubtful whether this incidence might have been appreciably increased, even if there had been more sections taken for microscopic study from the specimens which did not show the effects of chronic inflammation.

Nearly 15 per cent of the patients had had induced abortions and about 25 per cent previous laparotomies.

Decidual reaction in the stroma of the Fallopian tube was noted on 30 occasions, or 21.3 per cent. Recent studies on the early implantation of the human ovum support the conclusion that the development of decidua is an early effect of nidation rather than a cause.

Without entering into any of the theoretical or mechanical considerations of the etiologic factors, the information that we were able to obtain from our data is not so positive and specific as we had hoped it would be. However, it does place emphasis on the fact that in the greater number of cases the real cause of ectopic pregnancy remains obscure.

### Symptoms and Physical Findings

Because of the various pathologic courses that ectopic gestation may follow, the appearance, sequence or degree of intensity of the symptoms, and physical findings are more often atypical than not. Lower abdominal or pelvic pain, abnormal vaginal bleeding, a pelvic mass, and amenorrhea are the four cardinal manifestations of ectopic pregnancy.

Pain is the one symptom that is almost universally present. It was found in 98.5 per cent of our cases. In over half of the patients it was described as suddenly severe, sharp, or knifelike, and usually, under these circumstances, unilateral. The intermittent or cramplike and dull pains were, as a rule, localized in the lower abdomen. Pain alone made its appearance as the first symptom in 23.6 per cent of the patients in this series (Table IV).

TABLE IV. DAYS FROM LAST REGULAR MENSTRUAL PERIOD TO ONSET OF FIRST SYMPTOM (18 unknown cases excluded)

SYMPTOM	DAYS 0	1 TO 14	15 TO 28	29 TO 42	43 TO 56	57 TO 70	71 TO 79	TOTAL CASES	PER CENT INCIDENCE
Pain		1	4	9	10	5		29	23.6
Bleeding	5	4	7	25	7	1		49	39.8
Pain and bleeding	8	3	3	14	7	8	1	44	35.8
Vaginal discharge						1		1	0.8
Total cases	13	8	14	48	24	15	1	123	100.0
Per cent incidence	10.6	6.5	11.4	39.0	19.5	12.2	0.8		100.0

TABLE I. AGE INCIDENCE

AGE	TOTAL CASES	PER CENT INCIDENCE
19	2	1.4
20 to 24	19	13.5
25 to 29	41	29.1
30 to 34	41	29.1
35 to 39	34	24.1
40+	4	2.8
Total	141	100.0

TABLE II. GRAVIDITY PRECEDING PRESENT ECTOPIC PREGNANCY

GRAVIDITY	TOTAL CASES	NO. OF REPEATED ECTOPIC	PER CENT INCIDENCE
None	40		28.4
1 abortion	11	(1)	7.8
2 or more abortions	9	(2)	6.4
Ectopic	1	(1)	0.7
1 child	30		21.3
2 or more children	15		10.6
1 or more children and 1 or more abortion	35	(3)	24.8
Total	141		100.0

TABLE III. POSSIBLE PREDISPOSING FACTORS

FACTORS	TOTAL CASES	INCIDENCE
Infection	38	26.9%
Appendicitis	23	
Gonorrhea	4	
Pelvic Inflammatory Disease	4	
Tuberculosis	2	
Ulcerative Colitis	1	
Pelvic Infection Following Induced Abortion	4	
Induced Abortion	21	14.9%
Previous Laparotomies	35	24.8%

### Etiologic Factors

After surveying the factors that might be immediately or even remotely considered causative or predisposing, from the past and immediate history of our cases it can be concluded that in most instances the etiology is not clear. While it is easy to understand how endosalpingitis effected by gonorrhea predisposes a woman to ectopic gestation, it is indeed questionable whether this specific infection plays the etiologic role formerly attributed to it. Gonorrhea may be as widely prevalent today, but with the newer methods of therapy and their more prompt administration, the damaging results to the oviducts directly or indirectly caused by gonorrhea and by postabortal and postpartum infections may be prevented. Chemotherapy and the administration of penicillin will undoubtedly greatly alter the part that gonorrhea, in particular, and the pyogenic infections, in general, play in the etiology of ectopic pregnancy.

Inasmuch as pelvic and abdominal infections are generally considered to be the most frequent predisposing factors, Table III shows that in only 26.9 per cent of the cases a positive antecedent history of some inflammatory process was obtained that might be even remotely responsible for establishing the

is not present. On the other hand, one who is not alert to its possibility will meet with many surprises which greater care could have avoided." This quotation from Novak is aptly worded.

Preoperatively, the diagnosis was correctly made in 124 cases (87.9 per cent) of the 141 patients who were operated upon for ectopic pregnancy, and in whom the diagnosis was confirmed. In the remaining 17 cases the incorrect diagnoses were distributed as shown in Table VI.

TABLE VI. PREOPERATIVE DIAGNOSIS, NOT ECTOPIC PREGNANCY. ECTOPIC FOUND AT OPERATION

PREOPERATIVE DIAGNOSIS	CASES
Bilateral tuboovarian masses	1
Chronic pelvic inflammatory disease	3
Ovarian cyst with twisted pedicle	4
Ovarian cyst	3
Myoma uteri	5
Pelvic abscess	1
Total	17

In addition to our series of 141 cases of proved ectopic pregnancy, there were 95 women in whom the diagnosis of this condition was made or remotely entertained, but not found. Of these, 45 had laparotomies, 38 of which seemed justified (see Table VII), and seven unnecessary. Of the remaining 50 patients who did not have a laparotomy, 30 were subjected to an examination under anesthesia, at which time 22 were found to have an intrauterine pregnancy, while 20 had a dilatation and curettage, and in 13 of these an incomplete abortion ultimately proved to be the correct diagnosis.

Should one, therefore, consider not only the 141 patients with proved ectopic pregnancy, but also all those in whom this diagnosis was entertained, however remotely, we find that of the total 219 cases a correct diagnosis was made in 124 (56.6 per cent).

TABLE VII. PREOPERATIVE DIAGNOSIS, ECTOPIC PREGNANCY. ECTOPIC NOT FOUND AT OPERATION

POSTOPERATIVE DIAGNOSIS	CASES
Salpingitis	13
Subacute	5
Chronic	8
Hematosalpinx	6
Alone	4
With endosalpingeosis	1
Following Rubin's test	1
Ovarian cyst	13
Corpus luteum	7
Simple serous	3
With twisted pedicle	2
Endometrial	1
Myoma uteri	2
Adenomyosis	1
Hematocele	1
Retroversion	1
Acute appendicitis	1
Total	38

Abnormal vaginal bleeding was observed in 78.7 per cent in those instances where it could be accurately determined. Bleeding preceded the onset of pain in 39.8 per cent, while it was coincident with the onset of pain in 35.8 per cent of the cases (Table IV).

A pelvic mass was palpated in 99 patients, or 70.2 per cent of the total. In 14 patients pelvic examination was deemed unnecessary or hazardous in view of the typical history and other physical findings, and the acutely ill condition of the patient. In 19.1 per cent of the series no mass was felt.

Amenorrhea was reported by 64.5 per cent of the patients. The shortest period of amenorrhea was five days; the longest, eighty-two days.

The number of days that elapsed between the last regular menstrual period and the onset of the first symptom is also indicated in Table IV. In almost two-fifths of the patients, or 39 per cent, the first symptom appeared from four to six weeks after the last regular period. In 70 per cent of the patients, the first symptom was manifested in from two to eight weeks following the last period.

Weakness and faintness were recorded in 29.1 per cent, while collapse with shock was noted in 12.8 per cent in our series (Table V). Our experi-

TABLE V. WEAKNESS—SYNCOPE—SHOCK

PREOPERATIVE	TOTAL CASES	INCIDENCE
Weakness at onset of pain	12	29.1%
Fainted after pelvic examination	1	
Fainted at onset of pain	28	
Shock after an enema	1	12.8%
Shock after pelvic examination	3	
Shock at time of admission	14	
Total	59	

ence reveals that one patient fainted, and three promptly went into shock after pelvic examination. One sustained collapse with deep shock following an enema. About 10 per cent were admitted to the hospital in shock.

Among the more typical group of cases, twelve (8.5 per cent) complained of shoulder pain.

Nausea and vomiting, hemoglobin and hematocrit levels, red blood cell and white blood cell counts, sedimentation rate, fever, and rigidity of the abdomen are not present with any consistent or characteristic regularity. A persistent or increasingly rapid pulse and a relatively gradual fall in the hemoglobin and cell volume levels are more significant findings.

From these data one may conclude that pain, vaginal bleeding, the presence of a pelvic mass, and amenorrhea are pre-eminent in the history and symptomatology of ectopic gestation. While pain affects nearly every patient, abnormal vaginal bleeding most frequently appears as the first sign.

### Diagnosis

Ectopic pregnancy "may well be considered a disease of diagnostic surprises. The physician who has extrauterine pregnancy 'on the brain' will rarely fail to diagnose it when it exists, but he will diagnose it often when it



Mortality

There was one death in this series, or an incidence of 0.71 per cent. In the light of what is now known of the accidents and fatalities that may result from the transfusion of Rh-positive blood to an Rh-negative recipient, we feel that a brief summary of the case is warranted.

The patient, aged 36 years, para iv, gravida iv, with a history of cesarean section in 1933 for placenta previa, was admitted to the Woman's Clinic on Dec. 30, 1941, complaining of severe lower abdominal pain and syncope. Her last pregnancy was in 1938, when she was delivered of an erythroblastotic baby, icteric in type, that survived. The last menstrual period in her present illness was Oct. 26, 1941. There was a history of spotting beginning December 1 which lasted five days. Vaginal bleeding recurred on December 28. At 4:00 P.M. on December 30, she was seized with a sudden severe lower abdominal pain. She was in severe shock when admitted to the hospital. Preparations for transfusion were promptly made. She received 500 c.c. of citrated blood preoperatively and another 500 c.c. during the operation. Although her condition was critical throughout the operative procedure, some improvement was noted, and at the end of the operation her blood pressure was 95/70. On the first postoperative day it was observed that the urinary output was only 160 c.c., and on the second day she became jaundiced, with a urinary output of only 100 c.c. She failed to respond to all instituted therapeutic measures, gradually grew worse, and on the morning of the fifth postoperative day at 8:45 A.M. she died of pulmonary edema.

Even though at that time we were not yet testing our patients for the Rh factor, the history of an erythroblastotic baby in 1938, oliguria and jaundice following transfusion, and a terminal pulmonary edema strongly suggest the probability that this patient died because she received incompatible Rh blood.

Pathology

A brief review of the pathologic anatomy is pertinent. Every specimen in our series was carefully examined and described macroscopically and microscopically.

Special interest in the termination of tubal pregnancies prompted us to classify each specimen as accurately as possible. Tubal ruptures were easily segregated as a group. Great difficulty was encountered, however, in attempting to catalog the specimens in which the pregnancy was thought to have terminated as an abortion or as a result of internal rupture of the pseudocapsularis. If, in the presenee of a hematosalpinx, we found the ovum still attached to the implantation site, it was considered an instance of intratubal rupture of the pseudocapsularis. It is realized that more thorough studies, such as Litzenberg out-

TABLE VIII. CLASSIFICATION OF ECTOPIC PREGNANCIES

TYPE		CASES	INCIDENCE
Tubal		133	94.3%
Intact	1 ( 0.7%)		
Abortion	75 (53.2%)		
Intracapsular rupture	23 (16.3%)		
External rupture	34 (24.1%)		
Interstitial		5	3.6%
Secondary abdominal		2	1.4%
Intraligamentary		1	0.7%
Total		141	100.0%

For the most part, we have relied upon the history, symptomatology, and physical findings to arrive at the diagnosis. As additional diagnostic aids, posterior colpotomy was performed on only three occasions, and aspiration of the cul-de-sac on one occasion; in each case the findings supported the proved diagnosis. Pregnancy tests were utilized on 37 occasions and were of value in only a few cases.

Six patients passed decidual casts and 10 patients had a curettage before laparotomy. Six of this latter group corroborated the diagnosis, and four did not.

It is noteworthy that there were 25 cases, or 17.7 per cent, that did not have any demonstrable blood in the peritoneal cavity at the time of exploration.

Accordingly, our data show that the percentage of correct diagnosis is directly proportional to the character of each individual case. It is higher in the more typical cases, lower in the more atypical ones.

### Treatment

Torpin states that "an ectopic pregnancy is neglected if the operation is delayed more than a few hours after the first physician first sees her." This thesis may well be applied to those cases in which the diagnosis seems clear even though the operation is not an emergency. However, in the atypical case where the diagnosis is questionable or difficult, a more conservative approach and elective operation need no defense.

In determining the time that elapsed between admission to the hospital and operation, we learned that 24.1 per cent, or about one-fourth of the patients, were operated upon shortly after admission, and an additional 27.7 per cent within the first twenty-four hours. A total, then, of 51.8 per cent, or a little more than half of the cases in our series, had the operation on the day of admission. Within two days of admission, a total of 70.2 per cent came to laparotomy. After the fourth day, there were 22 cases that offered problems of differential diagnosis. Pelvic inflammatory disease was considered 10 times; threatened abortion, seven; and myoma uteri with infection or degeneration, five. The longest interval of time elapsing between the day of admission and day of operation was twenty-four days in a case of pelvic inflammatory disease with bilateral tuboovarian masses and unsuspected ectopic pregnancy.

There were 41 salpingectomies and 15 salpingo-oophorectomies performed on the right side, 38 salpingectomies and 26 salpingo-oophorectomies on the left, 16 bilateral salpingectomies and five cornual resections for interstitial pregnancies. A hysterectomy was indicated and combined with some of the above procedures on 11 occasions.

Transfusions were given to 60 patients, or 42.6 per cent of the total. Fifty (35.5 per cent) of them required it preoperatively or during the operation, and there were 19 in this group who, in addition, received transfusions postoperatively. Ten cases were given blood only after operation.

diagnosis in cases that are not emergencies, in cases which in any event generally require an exploratory laparotomy.

Pregnancy tests and dilatation and curettage are only of value in few selected instances, and even then are not always reliable.

There is no question but that the best treatment of this illness is surgical as soon as the diagnosis is established and as soon as the condition of the patient permits it. The generous use of plasma and blood transfusion cannot be too highly endorsed for the critically ill patient. The patient admitted in, or suffering from shock, at any time, should be moved to the operating room as soon as it is feasible, and measures to combat collapse promptly instituted or continued in the operating room. When the optimum moment presents itself, operation should not be delayed.

Williams and Corbit, in their analysis of fatalities from ectopic pregnancy, point out that hemorrhage and shock, as might be anticipated, caused the largest number of deaths. Infection was the next most frequent cause. The one fatality in our series, we believe, was the result of kidney shut-down caused by incompatible Rh blood. This accident sounds a note of warning. In extreme emergencies, the administration of plasma and antotransfusion can be utilized until compatible blood is made available.

While it cannot be determined with finality and completeness, our interest in the pathologic anatomy enabled us to obtain some idea of the manner and frequency in which ectopic gestation terminated. The greatest number of cases end as tubal abortions and about one-fourth as tubal ruptures. The attempt to evaluate the number of cases that terminated as internal ruptures of the pseudocapsularis revealed that 16.3 per cent could be so classified.

### Summary and Conclusions

1. The incidence of ectopic pregnancy, determined by a study of 141 cases in which the diagnosis was confirmed, is 0.34 per cent, or 1 in 293 pregnancies, at the Woman's Clinic of the New York Hospital.

2. Of the 141 cases of pathologically proved ectopic gestation, the diagnosis was made preoperatively in 124 cases (87.8 per cent). In a total of 219 patients in whom a diagnosis of ectopic pregnancy was entertained, the condition was found in 124 instances (56.6 per cent).

3. About one-fourth of the patients (24.1 per cent) were operated upon shortly after admission, 51.8 per cent within the first twenty-four hours, and 70.2 per cent within the first forty-eight hours after admission.

4. A total of 60 patients (42.6 per cent) received blood transfusions, 50 (35.5 per cent) preoperatively and during operation, and 10 (7.1 per cent) only after operation.

5. In this series, 94.3 per cent of the ectopic pregnancies were tubal, 3.6 per cent interstitial, 1.4 per cent secondary abdominal, and 0.7 per cent intraligamentary. Of the tubal pregnancies, 24.1 per cent terminated as tubal ruptures and 53.2 per cent as tubal abortions.

6. There was one death in this series, a mortality rate of 0.71 per cent.

lined in his valuable contribution to this subject, should have been done in order to make our evaluation more accurate and complete. Nevertheless, because there are no figures on the relative frequency of this particular termination of tubal pregnancy, our attempt does give some concrete idea of its incidence.

From Table VIII one learns that 94.3 per cent of the ectopic pregnancies were tubal, 3.6 per cent interstitial, 1.4 per cent secondary abdominal, and 0.7 per cent intraligamentary. Over half, or 53.2 per cent, of the tubal pregnancies were thought to have terminated as tubal abortions, 16.3 per cent as internal ruptures of the pseudocapsularis, and 24.1 per cent as external ruptures of the tube. One of the tubal pregnancies was considered to be still intact. It had not been anticipated that only about one-fourth of the cases would be classified as ruptured tubal pregnancies.

### Comment

Many of the facts that were revealed from this statistical study more or less conform to many of those that have already been reported and known. There are a few points, however, that should be briefly discussed.

The incidence of ectopic pregnancy and the age group in which it is more likely to occur, as well as the incidence of repeated ectopic gestation, are in general agreement with current statistics.

Without disputing the fact that infection may still be the most important and most frequent predisposing factor in the etiology, our data convince us that gonorrhea does not play the part formerly ascribed to it. Furthermore, it may be demonstrated in the future that the role of infection will be greatly altered as a consequence of chemotherapy and the use of penicillin. A review of all the factors that we considered possibly causative did not yield the information that we had hoped for. It only projected the fact that, for the most part, the etiology of ectopic pregnancy remains obscure.

Lower abdominal or pelvic pain, abnormal vaginal bleeding, a palpable pelvic mass, and amenorrhea reappear as the four cardinal manifestations of ectopic pregnancy. Whereas pain is nearly always present, in our series, vaginal bleeding more often appeared as the first symptom. It should be pointed out that collapse may follow too many or too vigorous pelvic examinations.

Not only was a correct diagnosis rate calculated in the cases in which ectopic pregnancy was verified, but also in those in which it was even remotely considered.

To arrive at the diagnosis, we have depended greatly upon an accurate history, the symptomatology, and physical findings. It is obvious that in the patients in whom the diagnosis is definite, there is no need for any accessory diagnostic aids. However, in those in whom it is presumptive and suspected, one might use aspiration of the cul-de-sac or posterior colpotomy a little more often. Even with these procedures, it is possible for one to be misled since, in our series, it was noted that there were 25 patients (17.7 per cent) without blood in the peritoneal cavity at the time of operation. We do not subscribe to the need for abdominal pneumoperitoneum, peritoneoscopy or aspiration through the abdominal wall. These procedures are usually employed for differential

tion of the fertilized ovum. There are many possibilities which will delay the migration of the fertilized ovum to the uterus and, if the delay lasts longer than six days, the ovum is going to implant itself, regardless of where it is—in the peritoneum, in the ovary, on the serosal surface of the uterus.

The other point I would like to discuss is that of patients who go into deep shock. Dr. Marchetti recommends that such patients be taken to the operating room and that appropriate methods be utilized to combat the shock and, once the patient has reached proper condition, operation can be performed. I believe that appropriate methods to combat shock should be instituted, but at the same time operation should be carried out, regardless of what the patient's condition may be. They do not require an anesthetic, they require oxygen, and they require the Trendelenburg position. As soon as the bleeding point is controlled, the patient rapidly comes out of the shock.

DR. HARVEY B. MATTHEWS.—I would like to ask Dr. Marchetti, why not separate the 141 proved cases into ruptured and unruptured ectopics? It has always seemed to me—and, of course, it is perfectly obvious—that the best time to treat ectopic is before rupture, and we believe that if the patient is seen early enough, the diagnosis can be made before rupture, and that certainly is more ideal than after rupture has occurred. So perhaps the doctor can give us some idea about those which were unruptured and those in which there was rupture at the time the patients were seen.

Dr. Marchetti stated that they do cul-de-sac puncture or needling in only a few cases. We believe that is out altogether. Nowadays, without better equipment and better diagnostic acumen, it seems to me that those two procedures for the diagnosis of ectopic gestation, ruptured or unruptured, are obsolete.

A point that I would like to take issue with him is the question of amenorrhea. We do not observe amenorrhea so often. I prefer to call it an abnormal period, or an abnormality in the sequence of the period, because some of the cases that the doctor showed were not really amenorrhea for the reason that they had gone only ten, fifteen or less days before they had symptoms of the ectopic, and I would not call that amenorrhea. You should call it an anomalous period.

In regard to the question of the time of operation, I agree with Dr. Marchetti and I do not agree entirely with Dr. Studdiford, because in our experience we have found that these patients recover and there is plenty of time for the operation before they go down again, and that is the time that Dr. Marchetti is talking about. I believe the kind of case that Dr. Studdiford has in mind is the interstitial. If you wait on those you do lose, or are very apt to lose, the patient. I think you will lose more patients if you work simultaneously with the shock treatment than if you wait until they recover somewhat and then begin to operate. You do not have many of the interstitial type; I think I have operated on only two patients with an interstitial pregnancy in my entire experience, where, as Dr. Studdiford says, they do not need an anesthetic they are so down and out; you operate with morphine only and then give 2,000 c.c. of fluid during and immediately after the operation, as was done in one of the cases, and the patient recovered. The other was years ago when we did not have blood transfusion and that patient died. But these patients always come back if they are not too far gone and you will save more of them by waiting until they come back than if you operate when the blood pressure is so low that it is hardly readable.

DR. NELSON B. SACKETT.—First, I would like the doctor's comment for and against resection of the tube instead of salpingectomy. I think I am echoing Dr. Ward in saying that resection of the tube is a very dangerous procedure, and that the worst case of interstitial pregnancy we ever encountered was such a case in which the tube had been previously treated by resection instead of salpingectomy. The patient had a nearly fatal interstitial pregnancy. I have had two patients, one of whom is in Dr. Marchetti's series, in whom an ectopic recurred on the opposite side in less than a year. Now the latter patient is most anxious for children, but has no tubes and one normal ovary.

In reference to etiological factors, I would like to ask Dr. Marchetti how many patients were found to have a simple retroversion.

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## Discussion

DR. CLAUDE E. HEATON.—I desire to present the figures for ectopic pregnancy from Bellevue Hospital. In a six-year period at that institution, we did 310 operations for ectopic gestation and found, as Dr. Marchetti did, that the diagnosis was often incorrect, for our percentage of failure was 29.7 per cent. The majority of our cases were ampullary, and we delayed considerably in operating on these cases. ✓

In contradistinction to Dr. Marchetti, we found that the Aschheim-Zondek test was of extreme value. In 60 per cent of our cases this test was positive. Furthermore, we lay great stress on the laboratory findings. The sedimentation rate was sixty minutes or over in two-thirds of our cases, and in less than 8 per cent of the cases it was less than thirty minutes. I might add that the white count was almost universally elevated. Therefore, a slow sedimentation rate with an elevated white count was of significance. ✓

I don't know what the difference is, but in spite of the general use of chemotherapy and penicillin we still meet with many cases of gonorrhea in the Bellevue Hospital Service. On microscopic examination we found in over 50 per cent of the specimens examined that there was no evidence of previous inflammation. ✓

We have also found that the curettage may be very misleading. Occasionally, however, the curette will clinch the diagnosis: I recall one case which was taken to the operating room and operated upon with a mistaken diagnosis. One of the interns had noted a patulous cervix. It would merely have required a preliminary inspection of the cervix and insertion of a sponge-stick to have made the diagnosis. On the other hand, when the curettage shows decidual tissue alone, that in itself may be misleading. We have found decidual tissue alone in a high percentage of incomplete abortions. However, we feel where there is a unilateral mass and a positive Aschheim-Zondek test that the diagnosis of ectopic pregnancy is almost universally correct. ✓

As far as I know, there was no mortality in our series.

DR. WILLIAM E. STUDDIFORD.—With regard to the question of obscurity of the etiology of ectopic pregnancy, I believe that anyone who has spent time on examining tubes after their removal in cases of ectopic pregnancy will find that a rather small proportion of them show any evidence of inflammation at all.

When you consider the etiology of ectopic gestation you have to remember the physiology which takes place during normal passage of the fertilized ovum into the uterine cavity. It is widely held, mostly on the basis of observations in animals, that fertilization takes place in the outer end of the tube. The ovum can develop right away and, during its migration from the outer end of the tube into the uterus, a lapse of time occurs of about four days. Therefore, there is a margin of safety of about forty-eight hours between the delivery of the ovum into the uterus and its ability to implant itself. You can say that the sole factor to account for the ectopic pregnancy is delay in fertilization and the time the fertilized ovum reaches its site of implantation. There are many reasons for that. For example, in a number of ectopics the corpus luteum is present in the opposite ovary and the tube in which the ectopic is found. The essayist has not given us any figures on the migra-

## ENDOMETRIOSIS IN ASSOCIATION WITH PREGNANCY

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ENDOMETRIOSIS has received much attention in the gynecologic literature since it was originally described by Russell<sup>1</sup> in 1899. Sampson,<sup>2</sup> in 1921, was the first to propose the theory of its etiology from implantation of endometrial fragments regurgitated through the Fallopian tubes during menstruation.

The apparent increase in the incidence of endometriosis has been distressing. Holmes<sup>3</sup> found 80 proved cases of external endometriosis in 307 gynecologic laparotomies, an incidence of 26 per cent. Sampson<sup>4</sup> has reported finding endometriosis in 43 per cent of abdominal operations performed on women between the ages of 30 and 50 years. Meigs<sup>5</sup> made a gross diagnosis of endometriosis in 36 per cent of 400 consecutive female patients at laparotomy, with pathologic confirmation in 28 per cent. Our experience with patients on the private gynecologic service of the North Carolina Baptist Hospital has closely paralleled that of this last group.

The literature has been concerned primarily with the etiology, pathology, diagnosis, and treatment of this disease. Although numerous series of cases have been reported and the gynecologic aspect of the condition has been fully discussed, the only obstetric factors which have received much consideration are the incidence of infertility and sterility, and the complications which may occur when pregnancy and endometriosis are associated. In 1944, however, Scott<sup>6</sup> reviewed the literature on endometriosis in pregnancy. He found only 47 reports of such cases, and added two of his own.

### Obstetric Complications

A brief summary of Scott's collected cases is given in Tables I to IV. Of the 31 patients in whom the probable ultimate result can be ascertained, two had spontaneous abortions and 10 had their pregnancy interrupted by operation (Tables I and II). Two of these patients had criminal abortions, and in two cases pregnancy was an incidental finding at operation. In one case operation was required for traumatic rupture of the uterus, which was probably not related to the endometriosis. Three ectopic pregnancies were found at operation; one (Sampson's) occurred in a patient who had had a tubal ligation, and another was a *left* ectopic pregnancy in a patient with an adenomyoma of the *right* uterine horn.

In 15 of the patients, delivery of a viable child was possible (Table III). Four of these were delivered by the vaginal route, and nine by cesarean section. In two cases the method of delivery was not stated. In two of the four

A third point is the matter of hematosalpinx. Dr. Plaut, formerly a pathologist at the Woman's Hospital, presented at our staff conferences on more than one occasion, cases of ectopic gestation in which the ectopic was confirmed after the gross and preliminary diagnosis was hematosalpinx; and he has made the point that without multiple, or even serial sections, it is well nigh impossible to exclude ectopic pregnancy as the cause of the hematosalpinx.

DR. MARCHETTI (Closing).—To answer Dr. Studdiford's question is precisely to do nothing but substantiate his discussion. Really, I do not think there is any argument or discussion about the role of mechanics as an etiological factor in this condition. There may be something intrinsic in the fertilized ovum itself, and we know that those things happen, but exactly to say what the real predisposing cause is I do not think is possible; or that one thing was the producing or causal factor for the mechanics that eventually ended in ectopic pregnancy. For example, it would be quite difficult to say: "Here are twenty tubes in which we found congenital diverticula of the tube." That is very difficult.

The other thing is that Dr. Matthews' remarks serve as corroboration. I don't mean to say that you should wait a long time, but as soon after a patient in shock begins to pick up, then the time of operation should not be delayed, and when there is a needle in the vein preoperatively, if the patient must be moved from some place to the operating room, it is advisable and really mandatory to have that connection in place, not to remove it, but to carry the patient with fluid and plan to give more fluid when she gets into the operating room.

I cannot answer Dr. Matthews' question as to how many of these cases were ruptured and how many were unruptured on admission. I could say about 30, but I am not sure of that. We know that at least 24 of the 124 were diagnosed as ruptured ectopic.

As to amenorrhea, I think Dr. Matthews is quite right about that. It is hard to say; we tried to determine. We just had to give it a name. You can call it an anomalous period if you wish. But in most of these instances there were some with a delay of ten or fifteen days in the next period, and they also had a previous irregular history. We threw those out, of course. A patient will say: "I have a 28-day period;" we know she does not have it regularly—it may be 26 days; or she may say that she has a 29-day period, so four days were excluded.

As to resection of the tube, I would say that, in general, we had three instances of cornual pregnancy in tubes which were previously resected, so I think it is less of a tragedy for the woman not to have her tubes, and perhaps not to be able to have a baby in the future than to run the risk of losing her from a serious ruptured cornual or interstitial pregnancy; that, too, in the case of patients who are anxious to have babies and who ask not to take out the opposite tube. If it is infected or there is any gross pathologic distortion, it is better if the opposite tube is removed. That may appear radical in some cases.

There was one patient in whom we were sure there was a retroversion. That was the only one we could find. At operation there were five cases in which the uterus was definitely retroverted.

The point about hematosalpinx is a good one. As I say, in all of these you cannot say whether the hematosalpinx is the result of the ectopic, that either has been completely ablated from the tube and absorbed in the peritoneal cavity, or whether it is hematosalpinx from some other cause. You may have noted that there were one or two associated with ovarian cyst with a twisted pedicle.



TABLE III

END RESULT OF ENDOMETRIOSIS AND PREGNANCY	LOCATION OF LESION			REMARKS
	INTER- NAL	EXTER- NAL	OTHER	
<i>Possible Viable Child:</i>				
<i>Vaginal delivery</i>				
Szenes <sup>23</sup>	+			Normal delivery, postpartum hemorrhage followed by vaginal hysterectomy.
Von Franqué <sup>13</sup>		+		Difficult forceps delivery with Dührssen's incisions in women in whom rectovaginal endometriosis previously diagnosed.
Szymanowicz <sup>24</sup>		+		Normal delivery, rectovaginal endometriosis previously diagnosed.
Scott <sup>6</sup>		+		Bilateral ovarian endometriosis. Right oophorectomy, left oophorocystectomy. Subsequent normal vaginal delivery.
<i>Cesarean</i>				
Hay <sup>25</sup>		+		Rectovaginal endometriosis. Two subsequent pregnancies, cesarean sections, one single, one set twins.
Batizfalvy <sup>26</sup>		+		Rectovaginal endometriosis. Subsequent pregnancy with cesarean section, hysterectomy at eighth month.
Portes, Varangot, and Francois <sup>27</sup>		+		Section hysterectomy at seventh month. Rectovaginal endometriosis by biopsy.
Lochrane <sup>28</sup>	+			Section for tennis-ball size adenomyoma and breech presentation.
DeJosselin and De Snoo <sup>29</sup>		+		Section for suspected cul-de-sac sarcoma found to be adenomyoma.
Sackett <sup>30</sup>	+			Repeat section. Adenomyoma present. Hysterectomy for uterine atony.
<i>Possible Viable Child:</i>				
<i>Cesarean</i>				
Olson and Hansmann <sup>31</sup>		+		Low cesarean section for contracted pelvis.
Scott <sup>6</sup>		+		Ruptured ovarian endometrial cyst. Cesarean section. Viable 2,280 Gm. child.
Schweitzer <sup>32</sup>	+			Section for placenta previa. Uterine atony. Adenomyosis found. Hysterectomy.
<i>End-result unknown</i>				
Griffith <sup>33</sup>		+		Rectovaginal endometriosis. Pregnancy normal one month from term.
Harbitz <sup>34</sup>			+	Endometrial cyst of abdominal scar four years after cesarean section. Subsequent pregnancy.

TABLE IV

END RESULT OF ENDOMETRIOSIS AND PREGNANCY	LOCATION OF LESION			REMARKS
	INTER- NAL	EXTER- NAL	OTHER	
<i>Ruptured Uterus:</i>				
Schäfer <sup>35</sup>	+			Para x, 7 months pregnant with twins. Lifted heavy weight. Ruptured uterus.
Stone <sup>36</sup>	+			Spontaneous rupture at onset of labor.
Richardson <sup>37</sup>	+			Spontaneous rupture at term. Decidual cell infiltration uterus.
<i>Death From Placenta Previa:</i>				
Williams <sup>38</sup>	+			Died from hemorrhage at sixth month from central placenta previa. Extensive adenomyosis found at autopsy.

TABLE I

END RESULT OF ENDOMETRIOSIS AND PREGNANCY	LOCATION OF LESION			REMARKS
	INTER- NAL	EXTER- NAL	OTHER	
<i>Abortions:</i>				
<i>Spontaneous</i>				
Vignes <sup>12</sup>		+		Spontaneous abortion at twenty-second week. Rectovaginal nodule excised.
Von Franqué <sup>13</sup>		+		Ovarian endometrial cyst removed in sixth week. Spontaneous abortion on thirty-eighth postoperative day.
<i>Operative</i>				
Ascheim <sup>14</sup>	+			Criminal abortion. Hysterectomy for rupture. Actual perforation not seen but adenomyosis found.
Schugt <sup>15</sup>	+			Criminal abortion at fourth month, uterus ruptured at digital completion of abortion; endometriosis found at site of rupture.
Peralta Ramos <sup>16</sup>		+		Continued vaginal bleeding after second criminal abortion. Endometrial cyst resected from right ovary.
Milnor and Tilden <sup>17</sup>			+	Therapeutic abortion for toxemia. Inguinal tumor removed. Diagnosis: endometrial cyst.
Rushmore <sup>18</sup>			+	Therapeutic abortion in woman who had increasing bleeding from cervix and an endometrial polypoid mass.

TABLE II

END RESULT OF ENDOMETRIOSIS AND PREGNANCY	LOCATION OF LESION			REMARKS
	INTER- NAL	EXTER- NAL	OTHER	
<i>Ectopic Pregnancy:</i>				
Cullen <sup>19</sup>	+			Unruptured left tubal pregnancy. Adenomyoma in right uterine horn.
Sampson <sup>20</sup>	+			Ectopic pregnancy in an area of endometriosis at left uterine cornu following an attempted tubal sterilization.
McKenzie <sup>21</sup>		+		Endometriosis and ruptured ectopie in same ovary. Patient also had eul-de-sac endometriosis.
<i>Incidental Pregnancy at Operation:</i>				
Sampson <sup>4</sup>		+		Intrauterine 14 mm. pregnancy and ovarian endometrial cyst found at operation for myoma uteri.
Amos <sup>22</sup>	+			Adenomyosis found at hysterectomy in five months' pregnancy.

vaginal deliveries, the labor was uncomplicated. In the two complicated cases endometriosis may or may not have contributed to the difficulties. In five of the patients cesarean sections were performed because of rectovaginal endometriosis or a mass in the obstetric pelvis; the indications in the remaining four patients were previous cesarean section, contracted pelvis, ruptured endometrioma, and placenta previa.

Spontaneous rupture of the uterus occurred in three patients (Table IV). In one of these cases numerous contributing factors unrelated to the endometriosis were present.

One patient (Table IV) bled to death from placenta previa at the sixth month of pregnancy.

change until approximately January, 1942. From that time until her initial examination here on Oct. 10, 1942, a progressive increase in the amount of menstrual bleeding and discomfort caused her to be confined to bed. Two or three days prior to the onset of the menstrual period, which began Sept. 30, 1942, she had noticed a slight brown discharge. During the following eight days the bleeding was so profuse that she used approximately 90 menstrual pads. There had been no associated metrorrhagia or leucorrhea. Neither she nor her husband had used contraceptives during their marriage.

The review of systems and the family and social histories was noncontributory. The only finding of significance in her past history was an operation for a ruptured appendix and peritonitis when she was 11 years of age.

The general physical examination revealed no abnormality. Pelvic examination showed a third degree retroversion of the uterus, which was fixed, irregular in contour, and much firmer than normal. Both ovaries were prolapsed into the cul-de-sac with the uterus. They were fixed in this position and were exquisitely tender. The original impression was chronic subinvolution of the uterus and chronic post-abortal pelvic inflammatory disease. The patient was advised to use the knee-chest position and hot douches daily.

During the next two months, two patient's symptoms became progressively worse, with an associated increase in size of the adnexal masses and the uterus. The diagnosis was then changed to pelvic endometriosis, and laparotomy was advised. This was performed on Jan. 18, 1943. The left tube and ovary were found to be fused into a cystic mass approximately 7 cm. in diameter, filled with a thick chocolate material, and densely bound to the adjacent peritoneum and viscera by adhesions. The right tube was normal, but the right ovary, approximately 5 cm. in diameter, contained a cyst filled with chocolate-brown material. The uterus was freed with some difficulty from the peritoneum of the cul-de-sac, and the posterior wall was found to be diffusely infiltrated with a thick material. In addition, there were three isolated nodules measuring 2 to 2½ cm. in diameter on the posterior-superior surface of the uterus.

Because of the patient's wish to have the childbearing function preserved, a total hysterectomy was not done. Instead, a left salpingo-oophorectomy and a fundectomy were performed, and the cystic cavity in the right ovary was evacuated, its wall destroyed with the actual cautery, and the ovary then closed with interrupted sutures of 000 chromic catgut. Approximately two-thirds of the corpus, including an estimated one-half of the endometrial cavity, was removed. The uterus was then closed with three rows of continuous 000 chromic catgut suture. The superior hypogastric plexus was removed.

The patient's postoperative course was uneventful, and subsequent pathologic examination of the excised tissue confirmed the diagnosis of adenomyosis, with associated external pelvic endometriosis. A pelvic examination seven weeks after operation revealed the uterus to be about half the normal size, in the anterior position, and freely movable. The right ovary was palpable, nontender, and approximately normal in size, shape, and consistency.

The patient was completely free of symptoms until January, 1944, when she again began to complain of dysmenorrhea. The pain was entirely localized to the lower right quadrant of the abdomen, and pelvic examination determined that it was associated with the right ovary, although no change in the size or consistency of this organ was observed. Her symptoms became progressively worse, and in May, 1944, the uterus was noted to be enlarged to the size of a six weeks' pregnancy and somewhat irregular in shape, with a rounded, tender nodule approximately 2 cm. in diameter on the right anterior wall. The use of irradiation was discussed with the patient and her husband, who elected to reserve such therapy until her symptoms were more severe.

In summary, it may be said that in only 9 of the 31 patients could an unfavorable course be attributed directly to the endometriosis.

The widely scattered group of isolated case reports summarized above has established the attitude which generally prevails regarding endometriosis and pregnancy. This attitude is typified by Haydon's<sup>7</sup> statement that "Extensive endometriosis is rarely associated with pregnancy. When endometriosis and pregnancy are associated, abortion, premature labor and extrauterine pregnancy may readily occur. In the presence of endometriosis and pregnancy, complications in labor are frequent. These may consist in rupture of the uterus, atony during cesarean section, or critical postpartum hemorrhage."

### Fertility and Endometriosis

In five reported series<sup>7-11</sup> comprising 2,078 cases of endometriosis (Table V), approximately 317 patients who were treated conservatively and could

TABLE V

AUTHOR	TOTAL CASES	FERTILITY REPORTED			OPERATIONS		FOLLOW-UP OF GROUP WITH PREGNANCY POSSIBLE		
							NUMBER	SUBSEQUENT PREGNANCIES	BABIES
		CASES	RELATIVE STERILITY	ABSOLUTE STERILITY	CONSERVATIVE	RADICAL			
Counsellor <sup>9</sup>	884	131	56.5%	32.1%	18.4%	81.6%	55	7	10
Payne <sup>8</sup>	307	238		40.0%	75.0%	25.0%	48	10	?
Haydon <sup>7</sup>	569	447	53.0%	38.0%				19	?
Keene and Kimbrough <sup>10</sup>	118	83	59.1%	40.9%	25.0%	75.0%	14	4	4
Turunen <sup>11</sup>	200				78.0%	22.0%	200	62	?
Total	2,078						317	102	14

reasonably expect to become pregnant were adequately followed up. One hundred two pregnancies were recorded for this group—an incidence of 32.5 per cent. Most of these authors advocated conservative therapy, but Table V shows that in two of the three series in which the figures can be accurately evaluated, radical procedures were employed in the vast majority of cases, conservative therapy being reserved for patients with localized lesions. Scott was sufficiently impressed by the frequency with which pregnancy follows conservative management of endometriosis to make a strong plea for preserving the childbearing function in these relatively infertile women.

One of us (FRL) has adopted an ultraconservative attitude in the management of young patients with endometriosis, many of whom are anxious to preserve their childbearing function. The extent to which this policy has been pursued is illustrated by the two cases reported below.

### Case Reports

CASE 1.—Mrs. V. A. C. This 28-year-old white woman was married in 1935, and had one pregnancy, terminating in an uncomplicated spontaneous abortion in March, 1940. A dilatation and curettage was done at this time. Subsequently she began to have dysmenorrhea, which persisted with little or no

The problem was discussed with the patient and her husband, and the decision made to institute conservative medical treatment. On Sept. 19, 1944, she was given testosterone (Metandren Linguets) to be taken 10 mg. daily until a total dose of 300 mg. had been ingested. Her next menstrual period began on Oct. 3, 1944, and the patient noticed an appreciable decrease in the amount of pain she experienced, but no corresponding reduction in blood loss.

The patient returned on Nov. 21, 1944, complaining of slight nausea, occasional vomiting, breast soreness, and urinary frequency. The uterus was appreciably larger and was asymmetrical, with a smooth, diffuse enlargement of the left anterior-superior wall. Hegar's sign was present. A diagnosis of intra-uterine pregnancy, complicated by adenomyosis and mild hypertension, was made.

The patient's prenatal course was uneventful, and her hypertension was successfully controlled by salt restriction and diet. On June 21, 1945, the blood pressure rose abruptly to 170/100, and the patient was admitted to the hospital. Labor was successfully induced by the administration of castor oil and progressed normally. A male child weighing 3,010 Gm. was delivered spontaneously in six hours. The third stage lasted five minutes, with spontaneous separation of the placenta, and a total blood loss of less than 100 c.c.

During the patient's prenatal and postnatal course she was entirely well, and was relieved of all the distressing symptoms which prevailed prior to her pregnancy. In September, 1945, she resumed her menstrual cycle. Examinations prior to this time revealed the uterus to be normal in size and consistency. In the three months which followed, however, the uterus grew steadily larger and became irregular in shape, and the patient had a progressive return of menorrhagia and dysmenorrhea. On Jan. 16, 1945, a total abdominal hysterectomy was performed. Pathologic examination of the uterus confirmed the clinical diagnosis of adenomyosis.

### Summary and Conclusions

Although the information contained in the medical literature leads one to believe that the combination of pregnancy and endometriosis is a dangerous one, we have reported two cases in which patients treated conservatively for endometriosis subsequently conceived and had a normal prenatal course, delivery, and puerperium.

Few specific case reports of uncomplicated pregnancies in patients with endometriosis are to be found, but a careful search of the literature reveals that such cases are mentioned casually in articles which deal primarily with the gynecologic aspects of endometriosis. An analysis of five such articles shows that approximately a third of the patients who are treated conservatively can successfully conceive, and indicates that the vast majority of such patients have a normal pregnancy. For this reason, we wish to re-emphasize the desirability of employing procedures which conserve the childbearing function in youthful patients with endometriosis.

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On Sept. 5, 1944, the patient reported that her last menstrual period had occurred on June 28. She had the usual symptoms of pregnancy, and a Friedman test was positive. The uterus, though of the same irregular contour, had increased considerably in size since the examination in May.

The patient's prenatal course was entirely uncomplicated. On April 16, 1945, eleven days after the expected date of confinement, she reported the onset of slight vaginal bleeding and was admitted to the hospital. The cervix was dilated 6 cm. and completely obliterated, and the head was in the right occiput transverse position below the ischial spines. Labor progressed rapidly, and a live normal female child weighing 2,780 Gm. (6 pounds, 2 ounces) was delivered by an elective low forceps procedure and episiotomy under cyclopropane and oxygen anesthesia. Spontaneous separation of the placenta occurred in twelve minutes, and the third stage was completed with a total blood loss of 150 cubic centimeters.

The patient left the city when her child was three months of age. She had not resumed menstruation, and was successfully nursing her baby. The pelvic findings were essentially unchanged from those recorded before her pregnancy. The uterus was the size of a five to six weeks' pregnancy and irregular in shape, with a rounded nodule approximately 2 cm. in diameter on the superior and anterior surface of the fundus. No palpable masses were present in the left adnexa. The right ovary was palpable, not tender, and within normal limits of size, shape, and consistency.

CASE 2.—Mrs. D. L. J. This 23-year-old white woman had not felt entirely well since the birth of her only child in November, 1937, following a normal pregnancy. She was consistently 10 to 12 pounds under her normal weight, became exhausted on average activity, and required rest periods throughout the day. She had had mild dysmenorrhea during her entire menstrual life. Her periods lasted four days and came at 21-day intervals. Within the past four months, however, she had had fainting spells associated with menstruation, very severe dysmenorrhea, and profuse vaginal bleeding during her entire period. Although no intermenstrual bleeding or leucorrhea had occurred, she had a light brown discharge for several days before and after menstruation.

The patient had numerous additional complaints such as low-grade fever, headaches, and insomnia, which were suggestive of a constitutional disease.

General physical examination was essentially negative, except for a moderate elevation in blood pressure. Pelvic examination revealed no gross abnormalities other than small healed lacerations of the cervix and a mild chronic cervicitis. The uterus was slightly larger than normal, but was smooth and symmetrical, in the anterior position, and freely movable.

Initially it was thought that the patient's menstrual complaints were probably related to a constitutional disease which was responsible for her low-grade fever and mild hypertension. She was therefore referred to an internist, and during the next two years numerous medical studies were made in an effort to ascertain the cause of her fever and elevated blood pressure. She was seen by us on three occasions during this interval, with no apparent change in the pelvic findings.

On Sept. 19, 1944, the patient reported that she had had no improvement in her menorrhagia, and that her dysmenorrhea had become progressively worse during the preceding three months, confining her to bed. At this time the uterus was found to be nodular, slightly tender, and enlarged to the size of a six weeks' pregnancy. Small masses were scattered throughout the uterine wall. The ovaries were found to be normal in size, shape, position, and consistency. A diagnosis of adenomyosis was made on the basis of the changing pelvic findings and the rather typical history.

## MANUAL REMOVAL OF THE PLACENTA; A BENIGN PROCEDURE

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NOT many years ago, manual removal of the placenta was considered one of the most dangerous and deadly procedures that obstetricians could be forced to perform, and the average mortality ranged between 10 and 15 per cent.<sup>1, 2</sup> Even as late as 1927, a large series reported from Wurzburg<sup>3</sup> revealed an uncorrected mortality of 8.2 per cent. Since 1940, the rate has dropped to roughly 1 to 3 per cent.<sup>1, 4-8, 10</sup> Undoubtedly the advent of chemotherapy and a stricter aseptic technique has been a significant factor in reducing both the mortality and the morbidity. The latter, however, still remains high (approximately 42 per cent)<sup>1, 6, 8</sup> in most of the current series reported. One gathers the impression that a moderate mortality and high morbidity are the inescapable accompaniments of manual removal per se. We have not found this to be so. It is the conditions associated with most manual removals, rather than the procedure itself, that have proved to be the cause. The following series is presented as evidence that manual removal is not the primary cause of postpartum mortality or morbidity.

### Material

The following 45 consecutive cases were all delivered in the relatively short period of two years, lending the advantage of unified control of procedure, by the same visiting and house staffs of the Massachusetts Memorial Hospitals. Two cases have been added because of their instructive features; one was referred to us three days post partum, and the other was followed in consultation at an outside hospital.

### Indications

The most important indications for manual removal were blood loss, retention of the placenta, and a desire to explore the uterus. Blood loss was the predominant indication. Excessive loss was the indication in 15 patients (33.3 per cent), and significant but not excessive loss in 22 patients (48.9 per cent). The criterion of significant and excessive blood loss has purposely been varied, since some patients tolerate blood loss much less readily than do others. Often the degree of tolerance can be correlated with the patient's size and general stamina. In any case, a falling blood pressure or a steady, even if not profuse, loss of blood has been taken as sufficient indication for manual removal, provided that the placenta cannot be immediately delivered by the usual methods. To wait for signs of beginning shock, or until a definite stated amount of blood has been lost, is to invite all the hazards attendant on any surgical procedure on a patient in or bordering on shock.

If the blood loss was profuse at any time, even immediately following the birth of the baby, manual removal was done at once. An approximate clinical estimate of the average amount of blood loss associated with this group is 350 c.c. Although this is well under 500 c.c.,<sup>1, 5</sup> the figure usually quoted for a blood-loss indication, it has been our experience, as pointed out above, that many patients just past the exhaustive efforts of labor cannot withstand even this amount of blood loss without seriously increasing the risks of manual removal, should

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TABLE I. ANALYSIS OF INDICATIONS FOR REMOVAL\*

INDICATION	CASES		AVERAGE TIME BEFORE REMOVAL	MINIMUM TIME BEFORE REMOVAL	MAXIMUM TIME BEFORE REMOVAL
	NO.	PER- CENTAGE			
Blood loss	15	33.3	8.1	0	28
Prophylactic for blood loss	27	48.9	14.1	1	33
Retention of placenta	8	17.8	51.7 (75.9)†	38	68 (245)†

\*Times given in minutes after delivery.

†One case was unusually prolonged owing to transportation time following delivery at home.

The series presented is divided between ward cases, handled under supervision by the residents, and private cases, delivered by the visiting staff. The procedure was identical for both groups, the only difference between them being that private patients remained in the hospital on the average of one day longer than did ward patients. Manual removal of the placenta was not found to increase the time of hospitalization in either group (Table III).

TABLE II. ANALYSIS OF CLINICAL DATA

	NO. OF CASES	PERCENTAGE
Mortality	0	0
Morbidity	1	2.2
Chemotherapy	22	48.9
No chemotherapy	23	51.1
Intravenous therapy	12	26.7
Shock	0	0
Subclinical shock	3	6.7
Uterine pack	5	11.1
Totals	45	100.0

TABLE III. AVERAGE HOSPITAL STAY (IN DAYS)

	WARD CASES		PRIVATE CASES		ALL CASES	
	NO.	AVERAGE	NO.	AVERAGE	NO.	AVERAGE
Nulliparous	5	9.2	13	10.5	18	9.8
Multiparous	21	8.2	6	8.3	27	8.2

### Mortality and Morbidity

No mortality was encountered in this series.

Morbidity, defined as a temperature rising to 100.4° F. or above on two consecutive days, was encountered in only one case (2.2 per cent). This patient was admitted in a morbid condition following the spontaneous home delivery of a macerated stillborn infant of seven months gestational age. She had a marked upper respiratory infection, with an admission temperature of 99.2° F., which was subsequently diagnosed as tracheobronchitis. Manual removal was indicated not only by placental retention, but also by persistent moderate bleeding, with a slowly falling blood pressure reading 92/82. The removal was done four hours after delivery, following a transfusion with 500 c.c. of whole blood. The postpartum course was also complicated by a recurrent pyelonephritis, as well as the tracheobronchitis. Thus, it seems reasonable to attribute the morbidity to a pre-existing infection rather than to the manual removal. This being the case, the corrected morbidity for the series would be 0.

### Gestational Age and Parity

The gestational age and parity were as follows: 35 patients (77.8 per cent) had full-term deliveries; 6 patients (13.3 per cent) were delivered in the third trimester of pregnancy; 4 patients (8.9 per cent) were delivered in the second

this have to be done. Without question, invasion of the uterus per se, without further blood loss, is enough to throw the patient into shock, if she is already in a borderline state of shock. It has, therefore, been our policy to resort to manual removal as a prophylactic measure whenever blood loss is persistent or threatens to become profuse, rather than to wait until it has become so and the obstetrician is forced to invade the uterus at a time when the patient is least able to withstand the procedure.

Retention of the placenta was the second most frequent indication for manual removal, occurring in eight cases (17.8 per cent). Without blood loss, forty-five minutes has been taken as the average length of time it is profitable to wait for separation to occur. Numerous authors<sup>9, 14</sup> attest to the fact that separation normally occurs within the first five minutes of the third stage, although expulsion of the placenta may be delayed for some time thereafter. If gentle suprafundic pressure twenty-five minutes after the end of the second stage did not result in delivery of the placenta, an extremely gentle application of the Credé method was employed. This was not repeated more than twice in the next twenty minutes, after which manual removal was done. That the Credé method be applied gently is imperative, since otherwise, like invasion of the uterus, it has a shocking effect on the patient, thus increasing the risk of shock at the time of the manual removal. Waiting longer than forty-five minutes before using the Credé method has been fruitless in our experience. After that time the cervix has usually contracted, so that expulsion without invasion of the birth canal is unlikely.

### Technique

The majority of all our deliveries are aided by episiotomy. On delivery, 10 international units of obstetric pituitrin is given intramuscularly. Local redraping is then done preparatory to repair of the episiotomy. If at any time the bleeding becomes profuse or is present as a steady continuous flow, the repair is interrupted and preparation for removal is begun. Otherwise, the repair is completed with the exception of tying the final knots or, in the case of the frequently used "no-knot" type of repair, it is completed to the point of the subcutaneous burying of the suture ends. By this method we have found that delivery of the placenta or manual removal can still be accomplished without damage to the repair. Frequently, spontaneous delivery of the placenta or signs of separation followed by expression of the placenta occur during the repair period. If delivery has not occurred, expression is attempted by suprafundic pressure when the repair has been completed, this usually being twenty to twenty-five minutes after delivery. If expression is unsuccessful and there is no notable bleeding, approximately twenty minutes is allowed to elapse, during which time two attempts to deliver the placenta by the Credé method are made. If the placenta still remains undelivered, the accoucheur changes his gown and gloves, the patient is kept under anesthesia and is completely redraped and repainted with antiseptic, and manual removal is done in the usual manner. Great care is always taken to identify the cleavage plane between the placenta and uterus before removal is attempted in order to rule out placenta accreta. A sterile Western strip is always at hand before the procedure is begun in the event that uterine packing becomes necessary. Ergotrate is withheld until the delivery of the placenta has been accomplished, when 1/320 grain is given intramuscularly. Uterine tone and hemorrhage following the removal are evaluated, and if there are any signs of atonicity or continued oozing of blood, a tight uterine pack is inserted. Transfusions and intravenous fluids are given as indicated at any time in the above procedure, but we have found that early manual removal before the patient has entered a state of borderline shock obviates their routine use (Tables II and VI).

down on the posterior wall of the uterus, accounting for the condition of the cervix. It was partially detached, and there was considerable bleeding from the placental site. A good cleavage plane was found between the adherent portion of the placenta and the uterine wall; the placenta was manually removed. The cervical and vaginal tears were rapidly repaired, controlling all hemorrhage. While the repair was in progress, the blood pressure began to fall, and a transfusion of 1,000 c.c. of whole blood was given. The blood pressure immediately began to rise, reaching its normal level four hours post partum.

Owing to the rapid identification and control of the sites of hemorrhage, in which manual removal of a partially separated placenta played an important role, and the immediate institution of antishock therapy, this patient never went into shock. The postpartum course was uneventful. The maximum temperature for the entire hospital stay was 99.4° F.

CASE 2.—A 28-year-old gravida iii, para ii, due to deliver on April 13, 1945, was admitted in early labor on April 7. There had been a slight show of blood, but the membranes were intact. The prenatal history had been entirely normal, with no bleeding at any time. The past history was noncontributory.

Physical examination revealed the fetus to be in the left occiput anterior position, the fetal heart rate was 149 per minute, and the head was in the mid-pelvic position. The cervix was dilated 2 cm. After an eight-hour labor, the patient was delivered with the aid of prophylactic low forceps. The infant was a vigorous, normal boy weighing 6 lb., 9 oz. Three-fourths of an hour before delivery the patient passed several dark blood clots, but there had been no bright red blood. Ten international units of pituitrin was given intramuscularly at the end of the second stage of labor. Immediately after birth there was a gush of bright red blood. The blood pressure, which had been 114/70 just before delivery, fell precipitously to 99/66. Preparations for manual exploration were made as rapidly as possible. The placenta was found to be partially separated, with a good cleavage plane under the adherent portion. It was removed manually two minutes after birth. Ergotrate,  $\frac{1}{320}$  grain, was given intramuscularly, and an intravenous injection of 1,000 c.c. of 5 per cent glucose in saline solution was started. As soon as the placenta was removed the hemorrhage notably abated, continuing only as a slow continuous trickle. The uterus did not become firm in response to the ergotrate. Therefore, a Western strip soaked in isotonic saline\* was used to tightly pack the uterus, after which another  $\frac{1}{320}$  grain of ergotrate was given, this time intravenously. All bleeding ceased, and the uterus became firm. A Foley retention catheter was inserted. Sulfadiazine was given orally, 1 Gm. every four hours, prophylactically. The pack was removed twenty-four hours later and there was no bleeding. The uterus remained firm. The maximum temperature during the 24-hour period while packed and in the following twenty-four hours was 99.6° F. The postpartum course was not remarkable, and the patient was discharged recovered on the eighth postpartum day.

This case serves to illustrate the cardinal principles of early interference in the event of abnormal bleeding, and the benign nature of manual removal and intrauterine packing, *if the patient is in good condition when the procedure is done*. Because there was no delay, the patient did not go into shock, did not require a transfusion, and did not run a septic, or even a morbid postpartum course, and the recovery period was not prolonged.

\*We have abandoned sulfonamide impregnation of uterine packs, since oral or intravenous chemotherapy is more effective than local and lends the advantage of accurate control of therapy by blood-concentration levels.

trimester of pregnancy; 18 patients (40 per cent) were primiparas; and 27 patients (60 per cent) were multiparas.

The only statistical change due to gestational age and parity is noted in the length of hospitalization. Nulliparas averaged 1.6 days longer in the hospital than did multiparas (Table III).

### Uterine Packing

Uterovaginal packing was resorted to in five cases (11.1 per cent). In none of these was a second packing required when the original pack was removed twenty-four hours later, although in each case preparations were made to do so before the pack was removed. Chemotherapy, in the form of sulfadiazine, 2 Gm. orally or 2.5 Gm. of the sodium salt intravenously, was started at once and continued every four hours, 1 Gm. orally with 2 Gm. of sodium bicarbonate, until the temperature had remained within normal limits for three days. The morbidity was not influenced by packing, although a slight rise in temperature was frequently noted toward the end of the twenty-four hour period. In every case, this returned to within normal limits immediately after the pack was removed (Table VI). We are not in agreement with some authors<sup>5, 10</sup> who state that packing not only greatly increases the morbidity rate, but also increases the incidence of severe puerperal sepsis.

TABLE IV. ANALYSIS OF PARITY AND GESTATIONAL AGE

NO. OF WEEKS	PARITY												TOTAL
	0	i	ii	iii	iv	v	vi	vii	viii	ix	x		
40+	14	11	3	3	1	1		1			1	35	
36+	1	1										2	
32+							1					1	
28+	2				1							3	
28	1	2	1									4	
Totals	18	14	4	3	2	1	1	1	0	0	1	45	

### Shock

No cases of true shock occurred in the series, but three cases of subclinical shock occurred, characterized by a rapidly falling blood pressure (Table II).

TABLE V. ANALYSIS OF CASES IN WHICH THE UTERUS WAS PACKED

CASE NO.	MAXIMUM TEMPERATURE		HOSPITAL DAYS
	WHILE PACKED	24 HR. AFTER PACKING	
307,641	98.6°	100.8°	8
310,251	100.0°	100.6°	13
301,732	99.2°	99.4°	12
310,561	100.2°	99.0°	8
315,239	100.0°	98.8°	11
Averages	99.6°	99.7°	10.6

CASE 1.—A 40-year-old gravida xii, para xi was delivered, by low forceps, of an 8 lb., 9 oz. infant after a short, easy labor. Immediately after birth there was a profuse flow of bright red blood. The patient was instantly prepared for manual examination to ascertain the source of bleeding. Two moderate-sized bilateral vault tears were found, with considerable oozing of blood. A small lateral cervical tear was also present, and bleeding from this point was profuse. The cervix was remarkably soft, friable, and engorged. The placenta was low

TABLE VI. ANALYSIS OF INDICATIONS FOR RECEIVING INTRAVENOUS THERAPY

	PROPHYLACTIC	SUBCLINICAL SHOCK	TOTALS
Infusion	5	1	6
Transfusion	4	2	6
Totals	9	3	12

TABLE VII. ANALYSIS OF CASES RECEIVING CHEMOTHERAPY

	CASES		MORTALITY	MORBIDITY	UTERINE PACKING	AVERAGE HOSPITAL DAYS	
	NO.	PER CENT				WARD	PRIVATE
No chemotherapy	23	51.1	0	0	0	7.1	9.1
Chemotherapy	22	48.9	0	1	5	9.1	10.0
Totals	45	100.0	0	1	5	8.1	9.5

Sulfonamides, usually sulfadiazine, were given prophylactically in 22 cases (48.9 per cent). Our usual dosage has been 2 Gm. for the first dose and 1 Gm. every four hours thereafter; this is varied after the first twenty-four hours according to the blood level of the drug, so as to maintain a level of 15 mg. per 100 c.c. Two grams of sodium bicarbonate were also given every four hours to alkalize the urine. The incidence of chemotherapy was higher in the earlier cases in the series, when it was routinely given to all patients. The later cases received it only if removal was particularly difficult or if a uterovaginal pack was inserted.

Penicillin was used in only three cases (7 per cent), with equally good results. It is expected that its use will be routine in the future for the majority of our cases in which chemotherapy is indicated.

### Additional Cases

Two additional cases are included because of their instructive features.

CASE 4.—A 25-year-old gravida iv, para iii was admitted to an outside hospital on Nov. 6, 1944. The prenatal course had not been remarkable.

After an uneventful labor, the patient delivered a healthy vigorous infant. The placenta was retained despite attempts to express it by suprafundic pressure. Blood loss was not marked at any time. An hour after the end of the second stage, several attempts to deliver the placenta by Credé treatment of the uterus were made, without avail. At this time there was a slight blood loss, noted as a slow continuous oozing from the vagina. There were no signs of separation of the placenta. Suddenly, during another attempt to deliver the placenta by the Credé method, the patient went into shock. All attempts to deliver the placenta were abandoned and antishock therapy was begun, this including transfusions of whole blood. In the next twenty-four hours the patient received 600 c.c. of plasma, 1,500 c.c. of whole blood, and 1,500 c.c. of isotonic saline solution, but remained in shock. Bleeding during this period was minimal except for the passage of occasional moderate-sized clots. On the second postpartum day she received 500 c.c. of whole blood and 500 c.c. of saline, after which she appeared to be in somewhat better condition, having partially rallied from shock. Forty-seven hours after delivery the placenta was expressed by suprafundic pressure, together with several large blood clots. Following delivery of the placenta, the patient's condition rapidly improved, and although the postpartum course was mildly morbid, it was not stormy. The maximum postpartum temperature was 101° F. The patient was discharged recovered thirteen days after delivery and eleven days after expulsion of the placenta.

CASE 3.—(Referred to above under morbidity.) A 24-year-old gravida iii, para iv, was admitted on March 23, 1945. She was due to deliver on May 28. Past history revealed "kidney disease" dating from the first pregnancy, which ended in delivery of an eight-month stillborn infant in 1939. The subsequent three pregnancies and deliveries had been uncomplicated. There had been no recurrence of the "kidney trouble."

The prenatal history was uneventful until two months before this admission, when the patient developed intermittent dysuria and pain at the left costovertebral angle. For the two weeks preceding admission, she also had a cough, productive of green mucopurulent sputum and associated with chilly sensations, feverishness, and sweating. She had not consulted a doctor throughout the prenatal course.

On the day of admission, the patient went into labor and delivered spontaneously a 1,540 Gm. stillborn girl at home without benefit of complete aseptic technique. She was admitted to the hospital two hours after delivery because of a retained placenta. Bleeding had been present only as an intermittent trickle from the vagina; two attempts to deliver the placenta by treating the uterus by Credé's method had been made an hour after delivery.

The pertinent findings of the admission physical examination were decreased tactile fremitus at the base of both lungs and fine, moist, crepitant rales over both apices posteriorly, and bilateral tenderness at the costovertebral angle, more marked on the left. The temperature was 99.2° F., the pulse 100, and the blood pressure 92/82. The red cell count was 3,800,000. and the hemoglobin 11 Gm. The urine showed a specific gravity of 1.024 and contained no albumin, olive sugar and 2+ ketones. The sediment was loaded with white cells.

Intravenous administration of 5 per cent glucose and saline was started immediately. After thorough preparation of the patient, manual removal was done four hours after delivery. The placenta was still adherent over approximately one-third of its surface, and a good cleavage plane was present. There was a 3 cm. succenturiate lobe along the placental margin. Following removal, a small amount of bleeding persisted and a tight intrauterine pack was inserted, controlling the hemorrhage. The infusion was followed with 500 c.c. of whole blood and 1,200 c.c. of electrolyte fluids containing 2.5 Gm. of sodium sulfadiazine. Sulfadiazine was continued orally, 1.0 Gm. every four hours. The blood pressure rose to 110/70 by the time the intravenous therapy had been completed, where it remained throughout the postpartum course. The pack was removed after twenty-four hours, and repacking was not required. The maximum postpartum temperature was 101.2° F., occurring on the second postpartum day. The patient continued to run a gradually diminishing, spiking temperature for the next five days, after which it remained normal. Her condition was diagnosed by medical consultants as a recurrent bilateral pyelonephritis, complicated by a subsiding acute tracheobronchitis. X-ray examination of the chest on the third postpartum day revealed peribronchial and perihilar infiltration and stippling throughout both lower lung fields. No acid-fast organisms were found in the sputum. The cough rapidly became nonproductive and disappeared on the sixth day. Culture of the urine revealed nonhemolytic *Staphylococcus aureus* and nonhemolytic streptococcus. The white cells disappeared from the urine sediment on the fifth day, and pain and tenderness at the costovertebral angle ceased by the seventh day. Pathologic examination of the placenta showed only focal calcification. The patient was discharged recovered on the thirteenth postpartum day.

#### Intravenous Treatment and Chemotherapy

In the total series, 12 patients (26.7 per cent) received either transfusion or infusion (Table VI). In the three cases described above, this treatment was given for subclinical shock. In the rest, it was given prophylactically.

was no appreciable bleeding at any time. The patient withstood the operation well, and the subsequent course, although morbid, was one of rapid recovery. The maximum postoperative temperature was  $101.6^{\circ}$  F., occurring on the third day, after which time it remained normal. The fundus descended to three fingerbreadths above the symphysis. The lochia was at first profuse and contained small fragments of necrotic placental tissue. The patient was discharged recovered on the twentieth postpartum day, twelve days postoperatively. She was followed by her local doctor but was seen by us twelve weeks post partum. During this period she had passed small fragments of necrotic tissue on two occasions without bleeding. At this time the uterus was only slightly larger than normal and the leiomyoma had shrunk to approximately 3 cm. in diameter.

Pathologic examination of the main portion of the placenta, as well as the fragments, revealed only focal calcification and infarction.

This case also illustrates the dangers attending too conservative an attitude toward manual removal. Had it been done early, the presence of the leiomyoma would have been much less of a handicap, owing to the then widely dilated cervix; the subsequent infection and generally poor condition of the patient would have been avoided; and the risk of sudden severe hemorrhage, always present while a placenta is retained, as well as the danger of a serious puerperal sepsis could have been prevented.

### Comment

The purpose of this paper is to make an ardent plea for earlier manual removal of the placenta while the patient is still in good condition to withstand the procedure. It is our impression that recent authors, although advocating earlier manual removals, still tend to procrastinate during the vital period for optimal removal. This is due to the too rigid interpretation of the indications for removal.

This series has amply demonstrated the relatively benign nature of the procedure per se. In our minds, the former morbidity and mortality associated with manual removal arises, not from the procedure, but from the usually associated excessive blood loss, the presence of definite shock with or without blood loss, and delays in removal, allowing supervening infection to begin. It has been pointed out that no definite quantity of blood loss should be relied on as an indication for manual removal, since the tolerance to blood loss is extremely variable, depending on many other factors, such as the length and exhaustiveness of labor, the suddenness with which the blood is lost, and the general stamina of the patient. Consequently, any steady flow of blood should serve as a warning that manual removal should be considered. Delay may waste the precious minutes during which this is possible, leading to consequences similar to those encountered in the additional cases described, as the unavoidable price of wishful thinking.

Since our technique is not unlike that generally used for manual removals, and since this series includes cases treated not only by visiting staff but by the house staff as well, the only logical cause for the improvement in mortality and morbidity in this series seems to be the radical changes in indications for the procedure that we have adopted.



This case amply illustrates the danger of shock from the combination of slow continuous blood loss and repeated and prolonged Credé treatment of the uterus. Failure to remove the placenta manually while the patient was still in good condition resulted in the sudden onset of shock. This precluded the possibility of manual removal and necessitated the prolonged and uncertain course of intensive antishock therapy, coupled with expectant waiting for separation of the placenta to occur, with all the attendant risks of superimposed infection and sudden profuse hemorrhage from the retained placenta.

CASE 5.—A 30-year-old gravida i, para i was admitted on Jan. 23, 1945, three days post partum. She had been delivered at an outside hospital of an 11 lb., 8 oz. normal, vigorous infant with the aid of low forceps and mediolateral episiotomy. Despite the large size of the baby, labor had not been difficult, lasting only six hours. Following delivery, the placenta was retained despite suprafundic pressure, followed by heroic Credé treatment of the uterus, which resulted in large ecchymoses of the abdominal wall. There was no vaginal bleeding, and only two small blood clots were passed in the three-day period before admission. A prophylactic course of sulfadiazine, in full therapeutic amounts, had been given at once. The past history was not remarkable.

Physical examination on admission was not remarkable except for ecchymoses of the abdominal wall and an enlarged uterus rising to the costal margin slightly to the right of the midline. The uterus was firm, slightly tender, and symmetrical. The temperature was 101.4° F. and the pulse 114. The urine was normal. The red cell count was 3,340,000; the hemoglobin, 9 Gm.; and the white cell count, 13,850, with 89 per cent polymorphonuclears. The total protein was 4.89 Gm. and the nonprotein nitrogen 24 mg. per 100 c.c.

The patient was obviously in no condition at this time to undergo any operative procedure, and all efforts were directed toward improving her general condition and the prevention of more serious infection. This required 5 days, during which time the patient received 1,500 c.c. of whole blood, 20,000 units of penicillin every three hours intramuscularly, and a high-protein diet. Pituitrin was also given in four courses, each course being composed of four doses at hourly intervals of 10 I.U. intramuscularly. Small necrotic fragments of tissue were passed on several occasions, being identified microscopically as placental tissue. The maximum temperature was 101.8° F., occurring on the day of admission; the remainder of the time it ran an irregular, spiking course between normal and 100.6° F. The urine was normal and blood cultures were negative.

Five days after admission and eight days after delivery, the fundus was at the level of the umbilicus, still slightly to the right of the midline, and there was a foul lochia. The temperature was 98.8° F., the pulse 96, and the blood pressure 118/78. The anemia and leucocytosis were essentially unchanged; the total protein concentration had risen to only 5.05 Gm. per 100 c.c. It was thought that to wait longer held little hope for improvement. Although hysterectomy is the usual procedure of choice in such circumstances, it might well have proved disastrous, owing to the patient's poor general condition. It was therefore elected to attempt manual removal, followed by hysterectomy if absolutely necessary.

On vaginal examination (the first that had been performed), under double setup precautions, a large intramural leiomyoma was felt in the lower uterine segment on the left. It was approximately 10 cm. in diameter and caused much difficulty in entering the uterine cavity. The placenta was found on the left lateral uterine wall and fundus. It was manually scraped off piecemeal with much difficulty, owing to the marked placental necrosis and the obstruction offered by the leiomyoma, making the placental site most difficult to reach. There



# THE RELATIONSHIP OF MATERNAL WEIGHT GAIN TO THE WEIGHT OF THE NEWBORN INFANT

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**M**OST physicians who supervise prenatal care caution their patients against excessive weight gain during pregnancy. Their reasons for doing so are multiple. It is the opinion of many that the size of the fetus may thus be controlled. Prevention of overgrowth of the baby, especially in the presence of a pelvic contracture, would reduce the incidence of disproportion with its attendant hazards.

Numerous contributions have been made to the literature concerning the relation of the maternal weight gain during pregnancy to the weight of newborn infants. Here, as in many subjects, controversial opinions have resulted from each author's analysis of his statistics. Davis,<sup>1</sup> Slemons and Fagan,<sup>2</sup> Bingham,<sup>3</sup> and Hanley<sup>4</sup> conclude that the birth weight of the newborn is proportionate to the maternal weight gain during pregnancy. Beilly and Kurland,<sup>5</sup> on the basis of a comprehensive mathematical survey of 979 cases, assert that a low, nevertheless significant, degree of correlation exists between the weight gain of the mother and the weight of the baby at birth. McIlroy and Rodway<sup>6</sup> aver that the infant's birth weight apparently is not directly dependent upon the maternal increase in weight. Chesley<sup>7</sup> clearly demonstrated the conflicting results encountered in a summary of 11,960 cases analyzed in the literature. In eight papers (5,799 cases), no significant difference had been observed between the weight gain of primiparas and multiparas; another eight (1,249 cases) found a greater gain in multiparas, whereas five (1,418 cases) found the reverse to be true. He stated that where differences are found, they are usually not very great, and probably not truly significant.

In the face of the many conflicting observations, a statistical analysis of a moderately large series of cases is warranted to throw further light on the relationship, if any, of maternal weight gain to the weight of the newborn infant.

## Material

During his tenure as Chief of the Obstetrics and Gynecology Section of a military hospital from May 20, 1944, to Nov. 29, 1945, the writer delivered 605 women of 610 babies. For the purpose of comparing the statistics covering these patients with those of other authors, 567 cases were selected for this survey based upon the following criteria:

1. Single pregnancies in which the patient began antepartum care prior to the twelfth week of gestation and was observed at regular intervals until term. In those instances in which patients transferred to this

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### Summary

Forty-five consecutive cases of manual removal of the placenta are reviewed.

All cases were delivered within the last two years, thus receiving the advantage of a unified policy of treatment.

The mortality was zero. The morbidity was 2.2 per cent, corrected to zero.

The technique of removal is not different from that used elsewhere.

The marked improvement in results, especially the lowering of morbidity, is attributed to the relatively better condition of the patient when the procedure is performed, which in turn arises from the radically liberal indications used for removal.

The benign nature of manual removal per se as a procedure is borne out by our results.

That complications arise from unwarranted delay is brought out by other current series in which early removal is endorsed but not fully enforced. Two additional cases are described to emphasize this point.

Since early manual removal performed on a patient in good condition is a benign procedure, radical liberalizing of the indications for it is in order.

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1. The mothers of the 10- to 15-pound group gained an average of 5.07 pounds more than the mothers in the preceding group, but the average birth weight of their babies was 2 ounces less than that of the babies in the smaller weight-gain group.

2. The average maternal weight gain of the 15- to 20-pound group exceeded that of the 5- to 10-pound group by 9.57 pounds. This increase in maternal weight gain was accompanied by a difference of only 1.25 ounces in the average birth weight of newborns of the respective groups. Comparison between the 15- to 20-pound and 10- to 15-pound groups reveals an increase of 4.5 pounds in the average maternal weight gain associated with a difference of 3.75 ounces in the average birth weights of the babies. In this instance, therefore, an increase in the average maternal weight gain which was one-half that noted in the preceding observations was associated with a difference in average birth weight which was three times as great.

3. The average birth weight of the babies in the 25- to 30-pound and 30- to 35-pound groups was the same, although a difference of 4.62 pounds existed between the average maternal weight gains of these groups. The babies averaged 3.25 ounces more at birth than those of the 20- to 25-pound maternal weight-gain group despite increases in the average maternal weight gain of 5.08 pounds and 9.7 pounds respectively.

4. The average birth weight of the babies of the 35- to 40-pound and 40- to 50-pound groups was identical. The average weight of the newborns of these groups was 1.25 ounces and 2.0 ounces less, respectively, as compared with that of the progeny of mothers of the two preceding groups. However, the increases in the average maternal weight gain had been marked.

Beilly and Kurland<sup>5</sup> concluded from their observations that there is a progression in the increase of the average weights of the newborns. They observed that with the exception of the 26 cases of the group where the mother had gained from 5 to 10 pounds, the average weight of the newborns paralleled the maternal weight gain. The statistics of the current series fail to substantiate this observation.

TABLE II. AVERAGE MATERNAL WEIGHT GAIN AND AVERAGE BIRTH WEIGHT

AUTHOR	NO. OF CASES	AVERAGE MATERNAL WEIGHT GAIN (LBS.)	AVERAGE WEIGHT NEWBORN	
			LBS.	OZ.
Davis <sup>1</sup>	150	21.00	7	4.5
Slemons and Fagan <sup>2</sup>	500	16.50	7	4.0
Hanley <sup>4</sup>	482	21.50	7	6.0
Beilly and Kurland <sup>5</sup>	979	22.28	7	3.0
Hannah <sup>8</sup>	236	13.20	7	13.0
Klein	567	21.05	7	6.0

Table II demonstrates the marked variations in the average maternal weight gain and the average weight of the newborn as determined by the individual authors.

These statistics suggest further evidence against the existence of a direct correlation between the average maternal weight gain and the average weight of the newborn. In the series in which the average maternal weight gain was the greatest (22.28 lbs.), the average weight of the newborn was the least (7 lbs., 3 oz.). The average weight of the newborn was greatest (7 lbs., 13 oz.) in the presence of the least average maternal weight gain (13.2 lbs.).

Clinic at a later period in pregnancy, antepartum records were obtained from the former physicians, thereby providing a complete record.

2. Onset of labor was spontaneous with delivery of a normal living infant.

3. With the exception of two well-compensated rheumatic cardiacs, the parturients had had no pre-existing disease.

The following cases were excluded from the survey for failing to meet the aforementioned criteria:

1. Prematurity	18
2. Elective cesarean section	5
3. Multiple pregnancy	5
4. Inadequate prenatal care	3
5. Stillbirths	3 (2 monstrosities)
6. Toxemia of pregnancy	2
7. Hodgkin's disease	1
8. Hemorrhagic disease of newborn	1
Total	38 cases

All patients were advised to partake of a well-balanced diet. However, each case was individualized. The obviously underweight were encouraged to increase the caloric intake to fortify themselves against the vicissitudes of pregnancy, parturition, and the puerperium. Those who presented evidence of being overweight or who were gaining weight too rapidly were admonished concerning dietary indiscretions. Most patients in this category adhered to the recommended diets. A few, however, were unable to resist gastronomic temptation.

TABLE I. MATERNAL WEIGHT GAIN AND WEIGHT OF NEWBORNS

MATERNAL WEIGHT GAIN IN LBS.*	NO. OF BABIES	PER CENT OF TOTAL	MATERNAL WEIGHT GAIN AVERAGE LBS.	AVERAGE WEIGHT NEWBORN LBS. OZ.	NO. OF MALES	AVERAGE WEIGHT OF MALES LBS. OZ.	NO. OF FEMALES	AVERAGE WEIGHT FEMALES LBS. OZ.
0-5	4	0.71	1.63	6 6.5	2	6 8.5	2	6 4.75
5-10	30	5.29	7.68	7 2.75	14	7 4.5	16	7 1.0
10-15	65	11.46	12.75	7 0.75	36	7 2.0	29	6 15.25
15-20	141	24.87	17.25	7 4.0	66	7 5.5	75	7 2.75
20-25	170	29.98	22.04	7 7.0	92	7 10.0	78	7 3.75
25-30	92	16.22	27.12	7 10.25	35	7 12.5	57	7 9.0
30-35	45	7.94	31.74	7 10.25	20	7 11.5	25	7 9.5
35-40	14	2.47	36.93	7 9.0	12	7 11.5	2	6 9.0
40-50	6	1.06	42.63	7 9.0	5	7 13.0	1	6 5.5
Entire series	567	100.00	21.05	7 6.0	282	7 8.5	285	7 4.0

\*0 lbs. up to but not including 5 lbs., etc.

### Observations and Deductions

I. *Maternal Weight Gain and Weight of Newborns.*—Table I is a presentation of the distribution of cases according to maternal weight gains in groups of 5 pounds ranging from 0 to 50 pounds, following the outline of Beilly and Kurland.<sup>5</sup> Each group tabulates the number of babies, percentage of the total, average maternal weight gain, average weight of newborn, distribution as to sex, and average birth weight of each sex.

Although the table indicates a tendency for the average weight of the newborn to increase as the mother gains more weight during gestation, it conclusively demonstrates that there is *no* proportionate relationship between the two. The evidence upon which this statement is based is as follows:

lbs.; (d), 13.93 lbs.—was associated with a difference of only 0.75 oz. in the average weights of the newborns—(b), 6 lbs., 4.5 oz.—(d), 6 lbs., 3.75 oz.

On the basis of these observations, it is difficult to accept the premise of Beilly and Kurland<sup>5</sup> that every one pound gain of the mother is accompanied by a 0.25 pound increase in the birth weight of the baby.

III. *Relation of Parity to Maternal Weight Gain and Weight of the Newborn.*—The statement was made in the introduction to this discussion that many controversial opinions have resulted from each author's analysis of his observations. This fact is emphasized when an attempt is made to establish a relationship between parity, the maternal weight gain during pregnancy, and the weight of the newborn. Bingham<sup>3</sup> determined that the average birth weight of babies of multiparas was 7 pounds, 6 ounces, whereas that of the babies borne by primiparas was 7 pounds, 3 ounces. Hannah<sup>8</sup> and Hanley<sup>4</sup> ascertained that primiparous mothers gained more weight during pregnancy than multiparas, but the reverse was true in regard to the birth weight of their respective progeny. Cummings<sup>10</sup> noted that primiparas averaged a greater weight gain than multiparas. Mellroy and Rodway<sup>6</sup> stated that "in primiparas an apparent correlation existed between the maternal weight gain and the birth weight of the infant, the latter being of greater weight as the maternal weight increased." Their results show that the maternal weight gain and the birth weight of the babies of multiparas exceeded that of primiparas. Siddall and Mack<sup>11</sup> and Bray<sup>12</sup> concluded that parity has little, if any, effect upon weight gain. The observations of the series under discussion are tabulated in Table IV.

TABLE IV. RELATION OF PARITY, MATERNAL WEIGHT GAIN, AND WEIGHT OF NEWBORNS

MATERNAL WEIGHT GAIN IN LBS.*	PRIMIPARA				MULTIPARA			
	NO. OF BABIES	PER CENT OF TOTAL	MATERNAL WEIGHT GAIN AVERAGE LBS.	AVERAGE WEIGHT OF NEWBORN LBS. OZ.	NO. OF BABIES	PER CENT OF TOTAL	MATERNAL WEIGHT GAIN AVERAGE LBS.	AVERAGE WEIGHT OF NEWBORN LBS. OZ.
0-5	3	0.53	1.75	6 4.5	1	0.18	1.25	6 13.0
5-10	25	4.41	7.84	7 3.5	5	0.88	6.85	6 14.0
10-15	45	7.94	12.84	7 1.75	20	3.53	12.55	6 14.75
15-20	111	19.58	17.29	7 3.25	30	5.29	17.03	7 7.0
20-25	121	21.33	22.03	7 6.5	49	8.64	22.07	7 8.75
25-30	60	10.58	27.21	7 8.0	32	5.64	26.91	7 13.0
30-35	30	5.29	31.44	7 8.5	15	2.64	32.33	7 14.0
35-40	9	1.59	36.56	7 6.5	5	0.88	37.60	7 13.75
40-50	4	0.71	43.06	7 8.25	2	0.36	41.75	7 11.0
Total	408	71.96	20.69	7 5.0	159	28.04	21.99	7 8.5

\*0 lbs. up to but not including 5 lbs., etc.

The 200 male newborns of primiparas averaged 7 pounds, 7.5 ounces as compared with an average weight of 7 pounds, 2.5 ounces for the 208 females. In the multiparous group, the average birth weight for the 82 males was 7 pounds, 9.5 ounces as compared with an average weight of 7 pounds, 7.5 ounces for the 77 females.

Although this table discloses that the average maternal weight gain and the average weight of the newborns of multiparas were greater than those of primiparas, the writer agrees with those authors who believe that where differences are found, they are usually not very great, and probably are not truly significant.<sup>7, 11, 12</sup>

IV. *Relation of Sex of Newborn and Birth Weight.*—Throughout this discussion, most results obtained have conflicted with those of other investigators. However, one respect in which the findings of this survey are in accord with the

II. *Relationship of Weight of Newborn to a Maternal Weight Gain of 20 Pounds.*—In discussing the subject of the relationship of the weight of the newborn to the maternal weight gain, some authors prefer to group their cases into categories based upon a maternal weight gain which is either less than or exceeds 20 pounds. Toombs<sup>9</sup> further subdivided these groups by introducing the factor of a 7-pound average weight of the baby. In Table III, a comparison is made between his findings and those of the current series.

TABLE III. RELATION OF WEIGHT OF NEWBORN AND 20-POUND MATERNAL WEIGHT GAIN

AUTHOR	TOTAL CASES	MATERNAL WEIGHT GAIN							
		20 LBS. OR MORE				LESS THAN 20 LBS.			
		BIRTH WEIGHT				BIRTH WEIGHT			
		(A)		(B)		(C)		(D)	
		7 LBS. OR MORE		LESS THAN 7 LBS.		7 LBS. OR MORE		LESS THAN 7 LBS.	
		CASES	PER CENT	CASES	PER CENT	CASES	PER CENT	CASES	PER CENT
Toombs	250	74	29.6	31	12.4	98	39.2	47	18.8
Klein	567	244	43.03	83	14.64	140	24.69	100	17.64

An analysis of Toombs' statistics discloses that, although 58 per cent of his patients had gained less than 20 pounds during pregnancy as compared with 42 per cent having gained 20 or more pounds, 68.8 per cent of the babies had weighed 7 or more pounds at birth. In the current series, 57.67 per cent of the mothers had gained 20 or more pounds (average 25.76 lbs.) as compared with 42.33 per cent whose weight gain had been less than 20 pounds (average 14.56 lbs.); 67.72 per cent of the babies weighed 7 pounds or more at birth (average 7 lbs., 14 oz.), whereas 32.28 per cent weighed less than 7 pounds (average 6 lbs., 4 oz.). The average weight gain of the 327 mothers who had gained 20 or more pounds was 25.76 lbs. The average weight of their offspring was 7 pounds, 8.25 ounces. The 240 mothers whose weight gain had been less than 20 pounds (average 14.56 lbs.) produced infants who averaged 7 pounds, 2.5 ounces at birth. Therefore, a difference of 11.2 pounds in the average maternal weight gain was associated with a difference of only 5.75 ounces in the average weight of the newborns.

Statistical investigation of the cases which comprise this series presents additional evidence against the existence of a direct correlation between the maternal weight gain during pregnancy and the weight of the newborn:

1. The average maternal weight gain of the cases in group (b) in Table III (25.88 lbs.) exceeded that of group (a) (25.64 lbs.) by 0.24 pounds. However, there was a difference of 1 pound, 10.5 ounces in the average weight of the newborns of the respective groups—(a), 7 lbs., 15 oz.; (b), 6 lbs., 4.5 oz.

2. The average weight gain of the mothers in group (e) (15.02 lbs.) was greater by 1.09 pounds than that of the mothers in group (d) (13.93 lbs.). The average birth weights of the babies of these groups differed by 1 pound, 9.25 ounces—(e), 7 lbs., 13 oz.; (d), 6 lbs., 3.75 oz.

3. The average weight gain for the group in which the mothers gained 20 or more pounds and whose babies weighed 7 or more pounds at birth was 25.64 pounds. The average weight of the babies in this group was 7 pounds and 15 ounces. The mothers whose weight gain had been less than 20 pounds and whose babies' birth weights averaged 7 or more pounds had gained an average of 15.02 pounds. The average birth weight of the babies of this group (7 lbs., 13 oz.) was only 2.0 ounces less than that of the preceding group, despite a difference of 10.62 pounds in the average maternal weight gain.

4. Concerning the babies whose average birth weight was under 7 pounds, a difference of 11.95 pounds in the average maternal weight gain—(b), 25.88

age maternal weight gain, parity, and the distribution according to sex are tabulated. Here, too, there is no evidence of a direct correlation between the weight of the newborn and the maternal weight gain during pregnancy.

### Summary and Conclusions

A series of 567 cases was studied statistically to determine whether any relationship existed between the maternal weight gain and the weight of the newborns. In this group of cases, 408 primiparas and 159 multiparas were delivered of 282 male and 285 female infants. The heaviest baby weighed 10 lbs., 7.25 oz. at birth; the lightest, 5 lbs., 4.5 oz. One mother who had lost 3.25 pounds during pregnancy gave birth to a 5 lb., 14 oz. girl. The patient who had gained the most weight, 48.25 pounds, was delivered of a 6 lb., 5.5 oz. female. The average maternal weight gain for the series was 21.05 pounds, with an average weight of 7 pounds, 6 ounces for the newborns.

Analysis of the statistics yields the following conclusions:

1. There is no correlation between the maternal weight gain during pregnancy and the weight of the baby at birth.
2. The average birth weight of males exceeds that of females.
3. There is no relationship between the age of the mother, her weight gain during pregnancy, and the weight of the newborn infant.
4. Although the average maternal weight gain and the average weight of newborns of multiparas were greater than those of primiparas, the differences were slight and of no significance.

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TABLE V. AVERAGE WEIGHT OF NEWBORN ACCORDING TO SEX

AUTHOR	NO. OF CASES	AVERAGE WEIGHT MALE		AVERAGE WEIGHT FEMALE	
		LBS.	OZ.	LBS.	OZ.
McIlroy and Rodway <sup>6</sup>	1,000	7	5	7	2
Beilly and Kurland <sup>5</sup>	979	7	5	7	0
Hanley <sup>4</sup>	482	7	10	7	3
Hannah <sup>8</sup>	236	7	15	7	6
Klein	567	7	8.5	7	4

results recorded in the literature is that the average weight of male newborns exceeds that of females. The results of this survey and the findings in other large series of cases are tabulated in Table V.

*V. Relation of Age to Maternal Weight Gain and Weight of Newborn.*—One of the purposes in reviewing the current series was to ascertain whether any relationship existed between the age of the mother, her gain during pregnancy, and the weight of her baby at birth. From the results tabulated in Table VI, the conclusion is drawn that there is no correlation between these factors. The older women apparently had gained the least weight but had had the heavier babies. The youngest mothers of the series were 16 years of age (two cases); the oldest were 37 years of age (two cases); 64.9 per cent of the mothers were less than 25 years old.

TABLE VI. RELATION OF AGE TO MATERNAL WEIGHT GAIN AND WEIGHT OF NEWBORN

AGE	NO. OF CASES	PER CENT OF TOTAL	AVERAGE AGE (YEARS)	MATERNAL WEIGHT GAIN AVERAGE LBS.	AVERAGE WEIGHT NEWBORN	
					LBS.	OZ.
15-19	55	9.70	18.30	20.5	7	4.5
20-24	313	55.20	22.00	21.6	7	5.75
25-29	146	25.75	26.60	25.4	7	5.75
30-34	46	8.11	31.90	20.5	7	9.5
35-40	7	1.24	36.00	19.2	7	6.0
Total	567	100.00	24.03	21.05	7	6.0

TABLE VII. DISTRIBUTION OF CASES ACCORDING TO WEIGHT OF NEWBORN

WEIGHT OF NEWBORN (POUNDS) *	NO. OF BABIES	PER CENT OF TOTAL	AVERAGE WEIGHT OF NEWBORN		MATERNAL WEIGHT GAIN AVERAGE LBS.	NO. OF PRIMIPARAS	NO. OF MULTIPARAS	NO. OF MALE	NO. OF FEMALE
			LBS.	OZ.					
5.0- 5.5	10	1.76	5	6.5	16.43	8	2	5	5
5.5- 6.0	27	4.76	5	11.8	18.11	21	6	9	18
6.0- 6.5	66	11.69	6	3.2	19.49	54	12	33	33
6.5- 7.0	80	14.11	6	11.8	20.00	55	25	35	45
7.0- 7.5	131	23.10	7	3.8	21.19	92	39	59	72
7.5- 8.0	98	17.28	7	11.75	22.33	74	24	46	52
8.0- 8.5	89	15.70	8	3.4	22.00	64	25	50	39
8.5- 9.0	45	7.94	8	11.4	22.11	30	15	31	14
9.0- 9.5	13	2.29	9	5.9	27.21	7	6	9	4
9.5-10.0	3	0.53	9	9.5	22.58	2	1	2	1
10.0-10.5	5	0.88	10	5.5	26.50	1	4	3	2
Entire series	567	100.00	7	6.0	21.05	408	159	282	285

\*5 lbs. up to but not including 5.5 lbs., etc.

Table VII represents the distribution of the cases of this series based upon 0.5 pound increases in the weight of the newborn. The average weight of the newborns, the number and the percentage of the babies in each group, the aver-



of adenomyosis uteri. In 1922, adenomyosis uteri was still considered enough of a rarity to report single cases as Abell<sup>6</sup> and Frank<sup>7</sup> did. Robins<sup>8</sup> reported two cases in 1923.

In the space of the last twenty years interest in the subject has grown tremendously, as indicated by an increasing number of papers.

### Incidence

Cullen,<sup>3</sup> McCarty and Blackman,<sup>4</sup> Westmann,<sup>5</sup> Light,<sup>32</sup> and Crossen and Crossen<sup>34</sup> found adenomyosis uteri in 5 per cent, 6.43 per cent, 8 per cent, 14 per cent and 5-6 per cent, respectively, of extirpated myomatous uteri. Frankl found internal adenomyosis (adenomyoma uteri) in  $\frac{1}{12}$  and Dougal<sup>24</sup> in  $\frac{1}{17}$  of their cases of fibromyomas.

On the other hand, Kanter, Klawans, and Bauer<sup>21</sup> found adenomyosis uteri in 52 per cent of 100 cases of myomatous uteri.

In reports on the incidence of uterine adenomyosis in all types of endometriosis, figures vary widely. Van S. Smith<sup>13</sup> found it to be 34 per cent; L. L. Hill,<sup>15</sup> 15 per cent; Cattell and Swinton,<sup>22</sup> 21 per cent; F. A. Pemberton,<sup>25</sup> 11 per cent; Counsellor<sup>27</sup> 69.9 per cent and F. L. Payne,<sup>35</sup> 6.5 per cent.

Shaw<sup>12</sup> reported at least slight adenomyosis uteri in all cases of endometrial hyperplasia, but Novak and Martzloff<sup>10</sup> found adenomyosis uteri in only 25 per cent of their cases of endometrial hyperplasia.

Meyer and Kitai found that a moderate degree of adenomyosis uteri was almost the rule in women approaching the climacteric.

Dreyfuss<sup>33</sup> found adenomyosis uteri present in 8.1 per cent of 1,870 uteri extirpated because of any lesion.

The difference in the incidence of adenomyosis as reported by various workers may be accounted for by the fact that slight "dipping down" of the endometrium into the myometrium is called adenomyosis by some, but ignored by others.

In this series, all cases of adenomyosis uteri were characterized by a marked downgrowth of endometrium in the muscular layer.

### Age Incidence

The works of Cullen,<sup>3</sup> Westmann,<sup>5</sup> Jeffcoate and Potter,<sup>16</sup> Roekstroh,<sup>20</sup> Skamnakis,<sup>28</sup> T. C. Moss,<sup>31</sup> Dreyfuss,<sup>33</sup> Fallas and Rosenblum,<sup>36</sup> and Frankl<sup>37</sup> all agree that by far the greatest number of cases of adenomyosis uteri occur in the fifth decade. (Table I).

TABLE I. PRESENT SERIES\*

Age	21-30	31-40	41-50	51-60	61 and up
No. of Cases	3	18	22	6	1
Percentage	6	36	44	12	2

\*Age range, 25-61 years; average age 42; age unknown in two cases.

In connection with the age incidence, it is interesting to note that Dreyfuss found the average age of his cases of adenomyosis uteri to be 46 years, while that of endometriosis was 33 years. This difference seemed to indicate to him different origins of adenomyosis and endometriosis.

The youngest case found is that of Holden<sup>14</sup> in a girl 14 years old, whose symptoms began six months after the onset of menstruation, and consisted of a severe dysmenorrhea. The adenomyotic tissue was within a definite fibroid, having no connection with the lining of the uterus.

This case would argue against those who believe, as does Dreyfuss<sup>33</sup> that repeated childbirths or abortions play a role in the genesis of adenomyosis.

## ADENOMYOSIS OF THE UTERUS

### A Study of 52 Reported Cases and a Review of the Literature

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A SERIES of 52 cases of adenomyosis uteri is presented in which the endometrium has been carefully studied. The preponderance of the anovulatory endometrium in this series (72 per cent) seems to indicate a definite association with this disease.

Despite a rather large volume of literature upon this subject, no definite general conclusions have been reached. Hofbauer<sup>30</sup> assumes the constant association of endometrial hyperplasia with adenomyosis uteri. Dreyfuss,<sup>33</sup> on the other hand, believes the endometrium exhibits a normal picture corresponding to the phase of the menstrual cycle in cases of adenomyosis uteri.

It is now generally accepted that the endometrium reflects the state of the ovary. The postmenstrual phase of the endometrium with its straight, tubular, nonsecreting glands is associated with follicular development. The early interval phase with slightly tortuous, nonsecretory glands, is associated with the well-developed follicle such as occurs immediately before ovulation. The late interval phase with moderately tortuous glands and epithelium with basal globules apparently indicates the presence of a young corpus luteum. The premenstrual phase with corkscrew glands and ragged epithelium accompanies the well-developed corpus luteum.

In probably 80 per cent of functional bleeding cases, either an interval nonsecretory endometrium, or endometrial hyperplasia ("swiss-cheese," cystic, nonsecretory endometrium) is assumed to be related to the lack of ovulation and the presence of follicular cysts in the ovaries.

It is rather generally accepted at the present time that endometrial hyperplasia indicates hyperestrinism. However, this point is still somewhat controversial.

In view of the fact that direct hormone titers are very difficult to determine and subject to many errors, endometrial findings are probably of more value, at the present time, in the study of abnormalities of ovarian secretion. In this series, the endometrial findings are classified, and the endocrine mechanisms are interpreted on this basis.

#### Historical

The work of Cullen,<sup>1</sup> in 1897, appears to be the earliest reference to adenomyosis in the English literature. He describes three cases and refers to earlier works of Von Recklinghausen and Dersterweig in the German literature. In a later paper, Cullen<sup>3</sup> mentions Von Rokitansky, who first described adenomyosis as a clinical entity in 1860. In 1902 Baldy and Longcope<sup>2</sup> reported two cases

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Most writers mention the fact that the age incidence of endometrial hyperplasia and adenomyosis uteri parallel each other. Both these conditions are most common in the fifth decade.

This relationship is further indicated by the similar incidence of adenomyosis uteri and endometrial hyperplasia in two series of myomatous extirpated uteri. F. W. Light,<sup>32</sup> in 100 myomatous uteri, found 13 had adenomyosis uteri and 17 had endometrial hyperplasia. Kanter, Klawans, and Bauer,<sup>21</sup> in 100 cases of myomatous uteri, observed 52 cases of adenomyosis uteri and 53 hyperplastic endometria. Neither of these papers mention how many patients had both of these conditions, so this data is not as significant as it might be. At any rate, a strikingly similar incidence of adenomyosis and endometrial hyperplasia is seen in both these series.

TABLE II.

	NO. OF CASES	NO. OF CASES OF HYPERPLASIA	NO. OF CASES OF EARLY INTERVAL ENDOMETRIUM	AVERAGE AGE
Group I	19	12	7	45 years
Group II	18	7	11	41.5 years

The present series of cases was studied in two groups, and the differences shown in Table II were noted in the course of the study. The table represents 38 cases in which hyperplasia or interval, nonsecretory endometrium was present. In one case the age was unknown.

The larger number of hyperplastic endometria in the older group and smaller number in the younger group led to further study of this situation. It was then found that the average age of the 19 cases with endometrial hyperplasia was 44 years, while the average age of those with an early interval nonsecretory endometrium was 37 years. This difference seems to indicate that the early interval nonsecretory endometrium is an early stage in the development of endometrial hyperplasia.

In the eight cases with secretory endometrium, the average age was 34.9 years, or almost seven years less than that for the whole series. It is possible that the process leading to endometrial hyperplasia has not been of sufficient duration to upset the menstrual cycle in these cases.

An interesting finding in one case was a mixed endometrium (secretory plus swiss-cheese, cystic hyperplasia). This patient was the only one in the entire series in whose ovary an active corpus luteum was seen. She complained of severe dysmenorrhea, but not of irregular bleeding. Her last menstrual period began sixteen days before operation.

Wilson and Kurzrok,<sup>26</sup> in an interesting discussion of the mixed endometrium, concluded that the most likely explanation of this phenomenon is excessive production of estrogenic hormone during the follicular portion of the cycle, producing a cystic endometrium to which secretory effects are added during the luteal phase of the cycle. Moreover, they produced a mixed endometrium in a woman with normal menses by prolonging and intensifying the follicular phase by means of estrogenic hormone. This is a peculiar and less common reaction than the purely hyperplastic endometrium, and its full significance is still unknown.

### Role of Hyperestrinism

Jeffcoate and Potter<sup>16</sup> conclude that an overproduction of estrin by the ovary is the most important factor in the development of endometriomas at any site.

### Symptoms

The symptoms of adenomyosis, per se, are very difficult to ascertain, because this lesion is so often associated with other pelvic pathology which may cause similar complaints.

Most writers agree that excessive irregular bleeding is the most common complaint; dysmenorrhea is much less frequent in adenomyosis uteri (Jeffcoate and Potter<sup>16</sup> and Dreyfuss<sup>33</sup>). In fact, Frankl found dysmenorrhea to be rare in adenomyosis uteri.

In the present series, patients complained of metromenorrhagia in 56 per cent of the cases. Dysmenorrhea was present in 29 per cent of the cases. Both together were present in 17 per cent of cases. Backache occurred in 3 per cent of cases.

In no case in this series was adenomyosis uteri present alone, therefore no definite conclusions can be drawn as to the symptoms of this condition itself.

### Endometrial Findings

The state of the endometrium in adenomyosis uteri is still a controversial point. Jeffcoate and Potter<sup>16</sup> found that endometrial hyperplasia occurred in 54.5 per cent of cases of adenomyosis and that the "interval phase" of the endometrium was a constant finding. Whether by "interval" they meant "early interval nonsecretory" is unknown. Frankl<sup>11</sup> found hyperplasia in 36.7 per cent of cases of adenomyosis uteri; Shaw,<sup>12</sup> in 100 per cent; Rockstroh,<sup>20</sup> in 17.4 per cent; Skamnakis,<sup>28</sup> in 13.2 per cent; and Dreyfuss,<sup>33</sup> in 13 per cent.

The difference between the various reports may be explained by the work of Burch, Phelps, and Wolfe<sup>17</sup> who find that where the specimens have been obtained after a long period of bleeding, one finds an early interval nonsecretory endometrium. This is hyperplastic in the sense that the endometrium is in the early interval phase, but should be in the secretory phase as determined by the last menstrual period. While these specimens do not exhibit the advanced morphologic changes of hyperplasia, clinical and experimental facts indicate that the changes shown are different forms of the same process and are to be classified with hyperplasia. If the interval nonsecretory endometrium occurring in what should be the premenstrual phase were classified with the hyperplastic endometrium, a much more common association of this condition with adenomyosis uteri might be found.

In the present series, the uterine endometrium was studied in 50 cases of adenomyosis uteri. Endometrial hyperplasia was present in 19 cases (typical swiss-cheese, nonsecretory endometrium). Early interval nonsecretory endometrium was present in 19 cases. In 12 of the latter cases, the endometrium, as reckoned from the last menstrual period, should have been in the secretory phase. In five cases, no last menstrual period was recognized or recorded. These cases are not included in the percentage tabulation, as their significance is unknown. In two cases, the nonsecretory endometrium was in the proper phase of the cycle, so that they were not necessarily significant and were, therefore, not included, either.

Thus, in 43 cases of adenomyosis uteri, there were three cases of senile endometrium, one case of "mixed endometrium," and eight cases of secretory endometrium.

The anovulatory cycle then was present in 31 cases, or 72 per cent. The anovulatory cycle (including endometrial hyperplasia and the sustained early nonsecretory endometrium) is accepted by most men as indicative of hyperestrinism (Jeffcoate and Potter<sup>16</sup>). Its occurrence in such large percentage may indicate that a causal relationship is present, or that both hyperplasia and adenomyoma have an identical etiologic factor.

available for study, and complete sections of ovaries and tubes were available in none of the cases.

The incidence of follicular cysts, as reported in the literature, varies from 3 per cent to 100 per cent. This difference may be at least partially explained by the fact that authors disagree on how large a follicle should be before it is called a cyst. Perhaps the minimum size of the cysts should be added to each report. In the present series only the largest follicles were called cysts in the tabulation.

The variation in the incidence of reported pelvic infection in cases of adenomyosis uteri is, likewise, very wide. This variation may be at least partially explained by the fact that the cases in each of the several series belonged to different strata of society. The greater prevalence of gonorrheal infection among the poorer people is well known.

Pelvic inflammation and follicular cysts are particularly important in connection with Witherspoon's<sup>19</sup> theory of the genesis of endometrial hyperplasia and adenomyosis uteri. He contends that inflammation prevents follicular rupture, leading to hyperestrinism and thus to endometrial hyperplasia and adenomyosis uteri. As a matter of fact, he found inflammation present in almost 100 per cent of his cases of adenomyosis uteri, so that his results bear out his hypothesis.

However, in the present series, inflammation was found in only 57.7 per cent of the cases. While this is a considerable percentage, it certainly does not bear out Witherspoon's theory. And it can be seen by the above table that very few papers on this subject noted such a high incidence of infection.

### Conclusions

1. Adenomyosis uteri occurs in 5 to 10 per cent of all myomatous uteri.
2. The uterine wall is the site of aberrant endometrial tissue in 15 to 30 per cent of all cases of endometriosis.
3. Adenomyosis uteri is most common in the fifth decade of life, as is endometrial hyperplasia.
4. Metromenorrhagia is the most common complaint, and dysmenorrhea second most common in patients with adenomyosis uteri.
5. The sustained interval nonsecretory endometrium is a part of the process leading to actual endometrial hyperplasia and should be classified with it. The early interval endometrium seems to occur in younger women and endometrial hyperplasia in older women, generally.
6. Adenomyosis is associated with anovulatory menstrual cycles in a large percentage of cases, indicating that either hyperestrinism or lack of corpus luteum hormone is an important factor in the genesis of adenomyosis uteri. It cannot be said definitely, however, which one is responsible.
7. The high incidence of fibroids in adenomyosis uteri seems to indicate some relationship. However, this association is not frequent enough to make one conclude that one factor is responsible for adenomyosis uteri and uterine fibroids.
8. Pelvic inflammation and ovarian cysts occur quite frequently in cases of adenomyosis uteri. However, the conclusion that these conditions are factors in the development of adenomyosis uteri does not seem justifiable.

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DeSnoo<sup>18</sup> feels that hyperfunction of the ovary causes adenomyosis and endometrial hyperplasia.

Witherspoon<sup>19</sup> says that fibroids, endometrial hyperplasia, and endometriomas are all due to excessive ovarian follicular hormone.

Moss,<sup>31</sup> on the other hand, concludes that hyperplasia of the uterine mucosa accompanies a large percentage of cases of endometriosis, particularly adenomyosis but that the hyperplastic endometrium in these cases differ from the usual picture found in excess secretion of folliculin.

Kanter, Klawans, and Bauer<sup>21</sup> feel that hyperestrinism plays a part in fibromyomas, adenomyosis, and endometrial hyperplasia, but that it is not the sole factor.

Sherwood<sup>29</sup> concludes that estrin is the activating principle in all endometriomas.

Light<sup>32</sup> concludes that endometrial hyperplasia, fibroids, and adenomyosis have a common etiologic factor, but that other factors must participate.

Henderson<sup>38</sup> feels that a disturbance in estrin production may be of etiologic significance in the production of adenomyosis uteri.

It is my opinion, from reviewing the literature and the present series of cases, that hyperestrinism, must often with absence of corpus luteum hormone, is a common factor, and probably an important one in endometrial hyperplasia and adenomyosis uteri. It is difficult to decide, however, whether a causal relationship is present.

### Incidence of Fibromyomas in Cases of Adenomyosis Uteri

Cullen,<sup>1</sup> in 1897, found that of three cases of adenomyosis, all had fibromyomas (100 per cent); Novak and Martzloff<sup>10</sup> found them in 62.5 per cent; Rockstroh,<sup>20</sup> in 70.5 per cent; Skamnakis,<sup>28</sup> in 53.8 per cent; Dreyfuss,<sup>33</sup> in 40.1 per cent; and Frank and Geist,<sup>39</sup> in 73 per cent.

In the present series of cases, fibromyomas were seen in 40.4 per cent, or 21 cases. This is a relatively high incidence and, in general, agrees with the incidence found by other men and seems to indicate some relationship between these two conditions.

Despite the opinion of DeSnoo<sup>18</sup> and Witherspoon,<sup>19</sup> it seems doubtful that hyperestrinism alone is the common cause of fibromyomas and adenomyosis, although they are probably associated in some manner.

### Other Associated Benign Pelvic Pathology

The following is a table of frequency of pelvic infections (including salpingitis, oophoritis, metritis) and ovarian follicular cysts in cases of adenomyosis uteri.

In the present series, although inflammation was seen in only 57.7 per cent of the cases and follicular cysts in 21.9 per cent of the cases, it must be kept in mind that in only 75 per cent of the cases were both ovaries and tubes

TABLE III.

AUTHORS	PELVIC INFLAMMATION	OVARIAN FOLLICULAR CYSTS
Cullen		33.3%
Baldy and Longcope	50%	
Frankl		3.3%
Shaw		100 %
Jeffcoate and Potter		57 %
Babes		60 %
Witherspoon	Almost 100%	
Rockstroh		5.8%
Skamnakis	14%	9 %
Present Series	57.7%	21.9%

## COMPLICATIONS AND FETAL MORTALITY IN 136 CASES OF MULTIPLE PREGNANCY

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THE general complications characteristic of twin pregnancy and the great importance of prematurity as the cause of the high fetal mortality in twin pregnancy have been emphasized by many investigators in this field.<sup>1-3, 6, 8</sup> The increased incidence of the toxemias of pregnancy, polyhydramnios, prematurity, uterine inertia, and postpartum hemorrhage has frequently been mentioned. In a large series of cases Hirst<sup>6</sup> has recently pointed out the increase in maternal, stillbirth, and neonatal death rates in cases of multiple pregnancy, and emphasized the problem of prematurity and the danger of hemorrhage. Hirst, therefore, emphasized the importance of diagnosis in cases of multiple pregnancy, and advised a high calorie and mineral diet, good general hygiene, early admission to the hospital, and avoidance of oversedation in labor.

Another aspect of the problem is the method of handling the second twin. McIlroy and Evans<sup>8</sup> advise extracting the second twin if any signs of fetal distress occur or if the interval is prolonged beyond an hour, because of danger of asphyxia from separation of the placenta. Beek<sup>2</sup> recommends rupturing the membranes after twenty minutes, and considers it a mistake to delay interference longer than one hour. Hirst advises more time up to one hour and fewer versions to allow the uterus to readjust itself in order to minimize the risk of infection and postpartum hemorrhage. DeLee and Greenhill<sup>3</sup> do not wait more than twenty minutes for the second baby to deliver spontaneously. They say, "there is little, if any, good in waiting, but many dangers—death of the second child, hemorrhage, and infection."

In the ten-year period ending May 31, 1944, there were 136 cases of multiple pregnancy delivered on the Obstetrical Service of Bellevue Hospital. Of these, 135 were twin pregnancies, and in one there were triplets. The incidence of twin pregnancy delivered during this ten-year period was 0.8 per cent. There was one maternal death in this series of 136 cases. An analysis of the prenatal courses, the labors, and puerperia of these 136 patients reveals a great difference in fetal mortality rates and in complications of pregnancy and labor between multiple and single pregnancies. The findings in these respects in the series coincide generally with previous reports on this subject.

### I. Fetal Mortality

The births, stillbirths, and neonatal deaths in this series are presented in Table I, which also compares the neonatal fetal mortality in multiple pregnancy and the death rates for all deliveries on the service during this period. The gross fetal mortality rate is tremendously increased in multiple pregnancy, being four times as great as in single pregnancy. Similarly, the corrected fetal death

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It is this factor of prematurity as illustrated by the low average birth weight and the small number of pregnancies progressing beyond 36 weeks of gestation that accounts for the high fetal death rate in multiple pregnancy.

### III. Presentations

The various combinations of presentations together with their respective incidences are presented in Table III. The most frequent combination was both

TABLE III. COMBINATION OF PRESENTATIONS OF FIRST AND SECOND TWIN IN 136 CASES OF TWIN PREGNANCY

PRESENTATIONS	NUMBER	PER CENT
Vertex-vertex	52	38.5
Vertex-breech	44	32.5
Breech-vertex	17	12.5
Breech-breech	10	7.4
Vertex-transverse	5	3.7
Vertex-compound	2	
Compound-breech	1	
Compound-vertex	1	
Breech-transverse	1	
Not determined	1	
	135	

being vertex presentations. Next most frequent was vertex-breech with the delivery being in this order. These two combinations accounted for 70 per cent of the cases.

### IV. Duration of Labor

There was no appreciable effect on the duration of labor in cases of multiple pregnancy. The average duration of the first stage was 11.8 hours for primiparas and 7.3 hours for multiparas. The average duration of the second stage was 68 minutes for primiparas and 39 minutes for multiparas. The third stage averaged 10.9 minutes for primiparas and 7.4 minutes for multiparas. The average time elapsing between the two births was 16.4 minutes in primiparas and 21 minutes for multiparas.

A comparison of some of the complications of pregnancy and labor in multiple pregnancy with those occurring in single pregnancy reveals some interesting facts. These are summarized in Table IV.

TABLE IV. THE COMPLICATIONS OF PREGNANCY AND LABOR IN 136 CASES OF MULTIPLE PREGNANCY AND IN 15,398 CONSECUTIVE DELIVERIES

COMPLICATION	IN 136 CASES OF MULTIPLE PREGNANCY		IN 15,398 DELIVERED PATIENTS
	NUMBER	PER CENT	PER CENT
Toxemias of pregnancy	22	16.0	5.7
Postpartum hemorrhage	16	11.7	5.5
Uterine inertia	11	8.1	3.0
Polyhydramnion	8	5.8	0.5
Prolapsed cord	8	5.8	0.73
Fetal distress	5	3.6	2.35
Premature separation of placenta	4	2.9	1.1
Placenta previa	2	1.4	0.44
Hypertension	2	1.4	
Retained secundines	2	1.4	
Hyperemesis gravidarum	1		
Retained placenta	1		
Cervical laceration	1		

TABLE I. THE GROSS AND CORRECTED FETAL MORTALITY RATES FOR MULTIPLE AND SINGLE PREGNANCIES IN A TEN-YEAR PERIOD

Total number of multiple pregnancies delivered	136
Total number of babies delivered	273
Total number of twin babies surviving	195
Deductible fetal deaths and stillbirths	53
1. Nonviable	42
2. Those with congenital abnormalities	5
3. Viable but macerated	4
4. Unrelated deaths	2
Nondeductible fetal deaths and stillbirths	25
Gross fetal mortality rate in twin pregnancy (General 10-year average for 15,398 deliveries = 7.0%)	28.1%
Corrected fetal mortality rate in twin pregnancy (General 10-year average for 15,398 deliveries = 5.5%)	9.1%

rate is higher, being about twice that observed in single pregnancy. The corrected fetal mortality rate was obtained by excluding stillbirths and neonatal deaths in which the birth weight was less than three pounds, deaths occurring in babies born with congenital anomalies incompatible with life, macerated stillbirths, and two deaths due to diarrhea on the tenth and twelfth days of life. There were 42 babies in the first group, those weighing less than 3 pounds at birth. It is this factor of prematurity that is the greatest danger the twin baby faces.

## II. Duration of Pregnancy and Birth Weight

The duration of pregnancy is summarized in Table II. Only 72, or 53 per cent, of the patients delivered had been pregnant for thirty-six weeks or more.

TABLE II. DURATION OF PREGNANCY

WEEKS OF GESTATION	NUMBER OF PATIENTS
40 or over	36
38-40	14
36-38	22
	} 53%
34-36	12
32-34	13
30-32	6
	} 23%
28-30	4
26-28	4
24-26	5
22-24	7
20-22	7
Under 20	4
Not determined	2
Total	136

The remaining 47 per cent were of less than thirty-six weeks duration of pregnancy, with 23 per cent being between thirty and thirty-six weeks, and 24 per cent being less than thirty weeks.

The average birth weight of the 273 babies born was 4 pounds, 7½ ounces. Only 116 babies weighed 5 pounds or more at birth. The largest baby born weighed 8 pounds, 10 ounces, while its twin weighed 7 pounds, 2 ounces. The mother of these twins died of a postpartum hemorrhage and was the only maternal death in the series; this case will be discussed in more detail later.

(e) Prolapse of the umbilical cord. This accident occurred eight times, an incidence of 5.8 per cent, as compared with a ten-year average for all deliveries of 0.73 per cent. The babies were saved in all these eight patients, except in one where the infants were nonviable. The corrected fetal mortality rate due to cord prolapse therefore was 0. This is due to the fact that the accident occurred in the second stage in all cases, and after the first baby had been born in all cases but one. The cause of the increased incidence of prolapse of the cord is that not only is there a higher incidence of malpresentation in multiple pregnancies, but also the second presenting part is frequently found well above the inlet with the cervix fully dilated. It is common to rupture the membranes of the second sac artificially after the first baby has been born. To avoid prolapse of the cord this artificial rupture should be delayed until there is enough adaptation of the presenting part to the inlet to minimize this danger.

(f) Less frequent complications of multiple pregnancy were fetal distress, premature separation of the placenta, and placenta previa. Although the percentage of incidence of each was slightly higher than in single pregnancies, the small values involved leave them with no significance.

There was one case of fetus compressus or papyraceous born with a viable, living twin in this series. There was no instance of locking of twins.

TABLE V. CORRECTED MORTALITY RATE FOR BOTH TWINS

Spontaneous delivery	9.5%
Operative delivery	14.1%

The viable fetal deaths in this series were further studied by comparing the corrected fetal mortality rate for twins delivered spontaneously with the corrected fetal mortality rate for twins born by an operative delivery. These values were 9.5 per cent and 14.1 per cent, respectively. The group delivered spontaneously had a somewhat lower death rate. Spontaneous deliveries included spontaneous vertex deliveries, spontaneous breech deliveries, and assisted breech deliveries. Operative deliveries included forceps deliveries, breech extractions and versions, and breech extractions. Cesarean sections were excluded from this calculation since, in all cases where cesarean section was performed, the indications for operation were in no way related to the fact that a multiple pregnancy existed.

The corrected fetal mortality rate for the first twin, when analyzed separately, revealed the fact that the death rate was higher in the spontaneous group than in the operative group. Of the 88 delivered spontaneously, 7, or 7.9 per cent, died. Of the 18 delivered operatively, one, or 5.5 per cent, died. Cesarean section deaths are excluded. In the spontaneous group there were five spontaneous vertex deliveries. The main finding at autopsy in all of these was prematurity; one case also showed subdural hemorrhage and another showed evidence of asphyxia. In this same spontaneous group were one spontaneous breech delivery and one assisted breech delivery; both showed prematurity at autopsy and the latter showed evidence of asphyxia in addition. This, however, was an intrapartum fetal death without maceration.

The fetal death in the first twin group delivered operatively was due to asphyxia.

## V. Acute Intra- and Postpartum Complications

(a) Polyhydramnion: This complication is 11 to 12 times more frequent in multiple pregnancy, the incidence being 5.8 per cent as compared with a ten-year average for all cases on the Bellevue Service (15,398 deliveries) of 0.5 per cent. This is not surprising when it is remembered that in multiple pregnancy there is a greatly increased surface of amnion as well as two fetal bladders to increase the amount of amniotic fluid.

(b) Toxemias of Pregnancy: Essential hypertension and hypertensive cardiovascular disease were not included in this classification which was limited to the mild toxemias, the unclassified toxemias, pre-eclampsia and eclampsia. Twenty-two of the 136 mothers, an incidence of 16 per cent, had some form of toxemia. This is almost three times more frequent than the ten-year incidence for all cases on the Bellevue Service of 5.7 per cent for the same complication. Of the 22 mothers, four had mild or unclassified toxemia, sixteen had pre-eclampsia, and two had postpartum eclampsia.

(c) Uterine inertia was more common in multiple pregnancy, being seen in 8.1 per cent of cases as compared with a ten-year average for all cases of 3.0 per cent. There was no correlation between uterine inertia and polyhydramnion, the two occurring together in only one instance. There was a relationship between inertia and postpartum hemorrhage, however, 25 per cent of the cases of postpartum hemorrhage also having uterine inertia. The overdistention of the uterus with resultant impaired contractility of the uterine muscle accounts for this increased incidence of uterine inertia. The greater the combined weight of the two babies the more likely it was that inertia would develop. Of the eleven patients exhibiting uterine inertia, the combined birth weight totalled well over 10 pounds in seven cases, and over 8 pounds in ten cases.

(d) Postpartum hemorrhage, that is,—a blood loss of 500 c.c. or over, was also more frequently encountered in multiple pregnancy, the incidence being 11.7 per cent as compared with a corresponding ten-year average for all cases on the Bellevue Service of 5.5 per cent. Throughout this period oxytocic drugs were used routinely.

Of the sixteen mothers having a postpartum blood loss of 500 c.c. or over, ten were multiparas and six were primiparas. Twenty-five per cent had associated uterine inertia, as already mentioned. There were two cases of associated polyhydramnion. This increased tendency toward postpartum hemorrhage where there had been overdistention of the uterus with subsequent poor contractility of the uterine muscle has long been recognized. The danger of postpartum hemorrhage in multiple births should always be kept in mind and should be especially anticipated if uterine inertia is associated.

There was one maternal death among these cases of multiple pregnancy, the cause being a postpartum hemorrhage of 2,300 c.c. This patient was a "grande multipara" who had already had 11 babies. She was delivered in 1936 of twins weighing 7 pounds, 2 ounces and 8 pounds, 12 ounces. Her labor of twenty-one hours was complicated by uterine inertia and a second stage of three hours. Both babies were delivered by breech extraction. The placenta failed to separate following delivery and had to be removed manually because of bleeding after a 45-minute third stage. This was during the period before the hospital had a blood bank, and the mother died before blood transfusions could be administered. Her babies developed diarrhea several days later and died, one on the tenth day of life and one on the twelfth day. These two infant deaths are not included in the corrected fetal mortality rate, but are the two unrelated neonatal deaths in Table I.

TABLE VII. ANALYSIS OF DEATHS AMONG FIRST TWINS

NAME	PARITY	WEEKS OF GESTATION	DURATION OF LABOR (HR.)	BIRTH WEIGHT (LB., OZ.)	PRES-ENTATION	COMPLICATIONS OF PREGNANCY AND LABOR	TYPE OF DELIVERY	INDICATION FOR OPERATIVE DELIVERY	CAUSE OF FETAL DEATHS
MG	1	34	1.3	3-1	V		Spontaneous vertex		Prematurity
RF	1	34	17	3-9	V		Spontaneous vertex		Prematurity; subdural hemorrhage
DH	2	40	35	3-8	Br	Fetal death Intrapartum	Assisted breech		Asphyxia; prematurity
IW	0	36	10.5	3-11	Br	Syphilis, morphine addiction	Spontaneous breech		Prematurity; incomplete expansion of lungs
MP	1	39	14.25	3-11	V	Toxemia of pregnancy	Spontaneous vertex		Prematurity (no autopsy)
RB	11	39	3	4-4	V	Postpartum hemorrhage	Spontaneous vertex		Asphyxia, prematurity, aspiration of amniotic fluid
RB	13	40	4.75	4-6	V	Polyhydramnion	Spontaneous vertex		Prematurity
HK	6	32	0	3-10	Br	Postpartum hemorrhage			
AA	0	32	22	4-9	V	Placenta previa	Cesarean section	Placenta previa	Prematurity
						Postpartum hemorrhage	Midforceps	Fetal distress	Asphyxia, nonexpansion of lungs

TABLE VI. FETAL MORTALITY ACCORDING TO METHOD OF DELIVERY OF FIRST TWIN

TYPE OF DELIVERY	TOTAL DELIVERED	TOTAL VIABLE AND NONMACERATED	VIABLE DEATHS
Spontaneous vertex	79	68	5 (7%)
Spontaneous breech	5	3	1 (33%)
Assisted breech	19	17	1 (6%)
Breech extraction	3	1	0
Version and extraction	1	1	0
Low forceps	14	10	0
Midforceps	6	6	1 (16%)
Cesarean section	5	3	1 (33%)
Complete abortion	4	0	0
	136	109	9
<i>Corrected Fetal Mortality for First Twin:</i>			
Spontaneous delivery	88		7 (7.9%)
Operative delivery (excluding section)	18		1 (5.5%)

These results are summarized in Table VI, and further details of each case of fetal death are presented in Table VII. The outstanding factor in these first twin deaths is the low birth weight further illustrating the great importance of prematurity as the major problem in fetal mortality in multiple pregnancies.

On analyzing the corrected fetal mortality rate for the second twins it was found that the spontaneous group had a lower death rate than the operative group, the figures being 12.5 per cent and 16.6 per cent, respectively. The four deaths occurring in the 29 viable spontaneous deliveries were attributable to asphyxia in three instances, to prematurity in one. There was an interval of thirty-eight minutes between twins one and two in one case. Both breech deaths were due to prematurity.

The operative group of the second twins had a corrected mortality of 16.6 per cent. Of twenty-one babies delivered by breech extraction five, or 23.8 per cent, died. Only one, or 4 per cent, of 25 viable babies delivered by version and breech extraction died. This peculiar discrepancy from the breech extraction death rate is accounted for by the fact that the average weight of the 21 breech extraction babies was 4.7 pounds, while the average weight of the 25 viable version and breech extraction babies was 5.45 pounds. The major cause of death at autopsy in all but one of the breech extraction babies was prematurity; the remaining one died of asphyxia. The one version and breech extraction death was due to prematurity; the indication for intervention in this case was malpresentation. Indications for operative delivery in the five cases of breech extraction were not given, although in one case the time elapsing since the birth of the first twin was over twenty minutes, and presumably the indication was no progress.

Three of the nine babies delivered by low forceps died, a 33 per cent mortality. Although prematurity was a major finding at autopsy in all three, brain hemorrhage was found in two instances. Prematurity was the indication for forceps in two cases, bleeding in one. Prematurity probably should not be considered an indication for forceps in the case of the second twin, since the birth canal has already been prepared for delivery by the passage of the first baby. This is borne out by the fact that these were the only two instances where pre-

TABLE IX. ANALYSIS OF DEATHS AMONG SECOND TWINS

NAME	PARITY	WEEKS OF GESTATION	DURATION OF LABOR (HR.)	BIRTH WEIGHT (LB., OZ.)	PRESENTATION	COMPLICATIONS OF PREGNANCY AND LABOR	TYPE OF DELIVERY	TIME BETWEEN DELIVERIES (MIN.)	INDICATION FOR OPERATIVE DELIVERY	CAUSE OF FETAL DEATH
CC	0	40	28.75	4-0	V		Spontaneous vertex	9		Prematurity
BT	i	36	6	5-8	V	1 loose loop of cord around neck	Spontaneous vertex	38		Asphyxia, incomplete expansion of lungs
MP	i	?	14.25	3-13	Br		Spontaneous breech	10		Prematurity (no autopsy)
AA	0	32	22	4-13	V	Fetal distress Postpartum hemorrhage	Spontaneous vertex	?		Asphyxia, nonexpansion of lungs
HG	0	39	5	4-4	V		Spontaneous vertex	15		Aspiration of amniotic fluid
VJ	0	33	3	3-11	Br	Anemia, pyelitis	Assisted breech	8		Prematurity
MB	0	36	8	6-0	Br	Toxemia of pregnancy	Breech extraction	5	None	Asphyxia (no autopsy)
ME	ii	32	3	3-12	Br		Breech extraction	20	None	Prematurity
MC	i	34	1.3	3-7	Br		Breech extraction	10	None	Prematurity
RF	i	34	17	3-9	Br		Breech extraction	11	None	Prematurity
JL	0	37	8.5	3-11	Br	Pulmonary atelectasis	Breech extraction	?	Not given	Prematurity, aspiration of amniotic fluid
CJ	0	34	11.5	3-10	Comp.	Polyhydramnion	Version and breech extraction	15	Compound presentation	Prematurity (no autopsy)
EH	0	41	25	4-9	V	Laceration of cervix; postpartum hemorrhage	Low forceps	4	Bleeding	Prematurity; brain hemorrhage
DH	ii	35	2	3-1	V		Low forceps	17	Prematurity	Prematurity; incomplete expansion of lungs
MM	0	33	12	3-11	V		Low forceps	18	Prematurity	Intracranial hemorrhage; prematurity
BW	0	40	9	3-8	V	Pre-eclampsia	Midforceps	?	Pre-eclampsia	Prematurity (no autopsy)

maturity was the indication for forceps delivery of the second twin, and death occurred in both instances.

One of the five babies delivered by midforceps died, a mortality rate of 20 per cent. The indication for forceps was pre-eclampsia.

These facts and further details in the case of each viable fetal death in the group of the second twins are presented in Tables VIII and IX.

TABLE VIII. FETAL MORTALITY ACCORDING TO METHOD OF DELIVERY OF SECOND TWIN

TYPE OF DELIVERY	TOTAL DELIVERED	TOTAL VIABLE AND NONMACERATED	VIABLE DEATHS
Spontaneous vertex	33	29	4 (13%)
Spontaneous breech	10	4	1 (25%)
Assisted breech	18	15	1 (6.6%)
Breech extraction	27	21	5 (23.8%)
Version and breech extraction	25	25	1 (4%)
Low forceps	9	9	3 (33%)
Midforceps	5	5	1 (20%)
Cesarean section	5	2	0
Complete abortion	5	0	0
	137	110	16
<i>Corrected Fetal Mortality for Second Twin:</i>			
Spontaneous delivery	48		6 (12.5%)
Operative delivery (excluding section)	60		10 (16.6%)

Although the corrected fetal mortality rate was higher in the group of second twins delivered by an operative route, analysis of the individual cases leads to the conclusion that the more important factor leading to fetal death was prematurity rather than the method of delivery. Any method of delivery, spontaneous or operative, is dangerous for a small, premature baby. However, since the fetal death rate was higher in the operative group, a further conclusion is necessarily that operative delivery should not be carried out prematurely, but only after giving the second twin time in which to deliver spontaneously unless bleeding or signs of fetal distress develop. The maximum time allotted for spontaneous delivery of the second twin by DeLee and Greenhill<sup>3</sup> is twenty minutes. Others give up to one hour. In this series the average time between twins was 16.4 minutes for primiparas and 21 minutes for multiparas. Where the second twin delivered spontaneously, the average elapsed time was 12.5 minutes. *Of those second twins allowed more than twenty minutes in which to deliver spontaneously, 63 per cent were eventually delivered by an operative method.* It would appear, therefore, that twenty minutes should be sufficient time to allow for spontaneous delivery of the second twin. Immediate intervention is indicated before this time if bleeding or signs of fetal distress occur.

### Summary and Conclusions

1. In 136 cases of multiple pregnancy delivered in ten years on the Bellevue Obstetrical Service, the gross fetal mortality was four times greater than the gross fetal mortality for all deliveries during the same period. The corrected fetal mortality for twins was almost twice as great as the ten-year average for all deliveries.



## A REPORT ON 2,798 VAGINAL HYSTERECTOMIES\*

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THIS report covers 2,798 vaginal hysterectomies for benign disease of the uterus performed at the Presbyterian Hospital, Chicago, by the attending† and resident staff. For comparison, this study has been divided into two groups; 1,361 (Group I) vaginal hysterectomies done by Dr. N. Sproat Heaney from 1922 through May, 1945, and 1,437 (Group II) done by the other members of the attending and resident staff from 1931 through 1944. In 1935, Heaney<sup>1, 2</sup> reported the first 627 cases in his total; these are included in this study with the additional 734 vaginal hysterectomies which he has done since that time.

With but minor individual variations, the technique developed and described by Heaney<sup>3</sup> has been followed in these operations. The technical procedures of this operation need not be reviewed in this discussion, but certain important points may well be re-emphasized. One of the most essential factors in any surgical operation is the decision as to the method of approach. The surgeon's ability to determine the safest and best anatomic and therapeutic means of correcting the pathology is as important to the patient as the technical skill of the operator. We feel that the reason that the resident staff has maintained a mortality rate comparable to that of the attending staff is largely due to the fact that we have insisted on adequate preoperative preparation and strict adherence to details of technique. We firmly believe that once the choice as to the proper method of removal of the uterus has been made by one experienced in these decisions, the mortality rate is affected very little by the difference in the manual dexterity of the surgeon. Under supervision, the residents have begun with simple vaginal hysterectomy and progressed through the more complicated procedures involving the removal of adnexal pathology or extensive repair. To substantiate this statement, we offer the comparison of these two groups.

It would seem only logical that the first and probably most important point in technique is the determination whether or not the pathologic conditions can best be corrected by the vaginal or by the abdominal route. Since most hysterectomies are done on multiparous women, some form of vaginal plastic is frequently indicated. If the vaginal route is not elected the operator has three choices: (1) a two-stage operation necessitating two hospitalizations, two anesthetics, and almost double the risk of a single major procedure; (2) a plastic operation followed immediately by a laparotomy which lengthens the operative and anesthetic time; (3) correction by laparotomy of the intra-abdominal pathology only, completely ignoring, as is so frequently done, the vaginal relaxation with its commonly associated condition of urinary incontinence. The patient certainly is entitled to a correction of all the pathology present by the best

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†Drs. N. Sproat Heaney, Edward Allen, A. E. Kanter, Fred O. Priest, Harry Boysen, C. C. Draa, Hugo C. Baum, Arthur H. Klawans, D. A. Rold, and Zeph. B. Campbell.

2. Prematurity was the outstanding cause for the greatly increased fetal mortality in multiple pregnancy. Only 53 per cent of the multiple pregnancies were carried beyond 36 weeks of gestation. The average birth weight was 4 pounds, 7½ ounces.

3. The order of frequency of various possible combinations of presentations has been presented.

4. There was no appreciable effect upon the duration of labor.

5. The toxemias of pregnancy, polyhydramnion, uterine inertia, prolapse of the umbilical cord, and postpartum hemorrhage were much more frequently encountered in multiple pregnancy.

6. The method of delivery of either twin was of secondary importance to the factor of prematurity insofar as fetal mortality was concerned.

7. Fetal mortality was higher in the second twin when delivered by an operative procedure. The second twin, therefore, should be allowed about twenty minutes for spontaneous delivery unless bleeding, evidence of fetal distress or maternal complications necessitate immediate intervention. It would not appear advantageous to wait longer than twenty minutes.

8. Prematurity should not be considered an indication for forceps delivery of the second twin.

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cinoma, 4.1 per cent of which occurred in the cervical stump. Meigs<sup>9</sup> reported 1,218 cases with an incidence of 2.13 per cent of the stump. Masson<sup>10</sup> reported 1,181 cases, with an incidence of 3.97 per cent. This gives an average incidence of 3.4 per cent of carcinoma occurring in the cervical stump in 6,668 patients having carcinoma of the cervix. In our opinion, such reports definitely indicate complete removal of the uterus by either vaginal or abdominal hysterectomy unless the immediate surgical risk of complete removal outweighs the chance of stump carcinoma. Vaginal hysterectomy is a distinct advance, in keeping with the increasing trend of most of the large clinics toward complete hysterectomy.

Waugh corroborates Averett's<sup>11</sup> observation that vaginal hysterectomy carries a lower mortality rate than does a menopausal dose of radium for benign lesions in the uterus. We subscribe fully to this statement and feel that selective vaginal surgery is far less radical than the frequently devastating effects of radium or x-ray with all of their sequelae on the female genitals and contiguous structures. Malignant changes which may occur in the functionless pelvic organs following irradiation are prevented by complete surgical removal.

We agree with the statements of many authors in dealing with hysterectomy that bad operative risks are better handled by vaginal hysterectomy. However, if vaginal hysterectomy is a safer procedure for bad operative risks, should not it be by far the safest one for good operative risks? Therefore, we feel that the contraindications for vaginal hysterectomy should be less rigid.

### Contraindications to Vaginal Hysterectomy

In view of our indications given above, it is obvious that our contraindications are much less rigid than those proposed by most surgeons. We believe that the only fundamental contraindications to vaginal hysterectomy are conditions which obviously would increase the risk of vaginal over abdominal removal, or the presence of additional intra-abdominal pathology requiring a laparotomy. The size, position, mobility, and accessibility of lesions are so variable that no indication or contraindication should be considered unchangeable. The bulk of a uterus to be removed is probably less a contraindication than is the location of its component parts. A large fibromyoma situated in the cul-de-sac or on the fundus can frequently be removed more easily than can a small tumor located directly beneath the bladder or between the leaves of the broad ligament. Tumors in the latter location, even though small, may greatly interfere with the securing of the uterine arteries.

Heaney<sup>2</sup> and Babcock<sup>12</sup> have demonstrated that large fibromyomas may be safely removed by morcellation if the uterine vessels have first been ligated. Morcellation is a tedious procedure for the surgeon, but the accumulated reports of vaginal hysterectomy demonstrate that it should not be denied the patient out of consideration for the operator. The site of a tumor growth may somewhat limit the mobility of the uterus but complicating pathology, such as endometriosis, chronic pelvic infection, and diverticulitis of the colon, are much more apt to produce insurmountable fixation. Ovarian tumors of large size associated with uterine pathology usually contraindicate vaginal hysterectomy. This is especially true if the ovarian enlargement is suggestive of malignancy; however,

and safest method that does not increase the surgical risk. The method chosen should be based upon this consideration alone and not upon the comfort, convenience, or limitations of the surgical team.

### Indications for Vaginal Hysterectomy

We are firmly convinced from our observation of the patients in this series, that when a hysterectomy is indicated the vaginal route affords by far a lower mortality, morbidity, and a better final surgical result than the abdominal route. There is also much less postoperative discomfort. This is attested to again and again by patients who have undergone previous abdominal surgery. We agree with H. O. Jones<sup>4</sup> in his discussion of a paper on hysterectomy by Philip H. Smith,<sup>4</sup> in which he states that "measuring the discomfort by the amount of postoperative sedation, vaginal hysterectomies require 25 per cent less than do abdominal hysterectomies." Abdominal incision with its subsequent scar produces more discomfort and psychic trauma to the patient than does an incision concealed in the vaginal vault. Atelectasis, pneumonia, and other pulmonary complications are less frequently encountered following vaginal operations because there is no abdominal incision to splint the abdomen and interfere with excursions of the diaphragm. We agree with Waugh<sup>5</sup> that thrombophlebitis is much less common because of the decreased trauma to the large pelvic veins. There were only four cases of definite thrombophlebitis in our series. We believe that the incidence of pelvic abscess and pulmonary embolus is less frequent for the same reason. However, we also believe that there is another contributory factor in the decrease in these infectious processes, namely, preoperative elimination of foci of infection. This point will be discussed in more detail under preoperative preparation of the patient. In the rare instances where pelvic abscesses do occur, we have encountered no difficulty in adequately draining them through the vaginal incision. The danger of injury to the bowel by actual perforation or by the use of a large abdominal pack is definitely less in vaginal surgery, and therefore the risk of postoperative adhesions, ileus, and bowel obstruction is minimized. Gas pains are less severe for these same reasons.

We have had no experience in removing the uterus by the clamp method described by Kennedy,<sup>6</sup> in which he emphasizes the increase in the length of the vagina over that when mass ligation of vessels is practiced. We have never been able to understand the common belief that the vagina is shorter after vaginal than after abdominal hysterectomy. If the severance point of the vagina is the same in each case, how can the route of the removal of the uterus make any difference? When a woman has a large prolapse the vagina is shorter than usual, and will be short whether the uterus is removed vaginally or abdominally. We feel that the relatively minor shortening of the vagina following total hysterectomy by any method that may be used adjusts itself very rapidly under the pulsion stress of intercourse. We have all observed this deepening in the production of artificial vaginas as epitomized by Frank<sup>7</sup> in his reported cases. Gynecologic literature is replete with reports of carcinoma of the cervical stump following subtotal hysterectomy. Von Graff<sup>8</sup> reported 4,269 cases of cervical car-

in this way covers all raw areas and places the stump extraperitoneally. When the suture is continued through the peritoneum of the cul-de-sac of Douglas and out through the posterior vaginal mucosa, the vessels are doubly ligated and the peritoneum is closed tightly as the suture is tied.

We have all felt that some of the most difficult cases in this series were those undertaken for the cure of prolapsus uteri. The extensive dissection necessary to correct the commonly associated pathology of cystocele, urethrocele, and enterocele frequently makes this operation extremely technical. Due to the displacement of the bladder, ureters, and rectum, there is an increase in the possibility of injury to these structures. Our residents in their training for vaginal surgery advance from hysterectomy in the nullipara or virgin to the more difficult cases of prolapsus uteri. As indicated above we do not subscribe to the general statement that nulliparity is a contraindication to vaginal hysterectomy. This is a direct contradiction to the idea advanced by many men that a considerable amount of pelvic relaxation must be present in order to make a vaginal hysterectomy permissible. Even in virgins, sufficient exposure can usually be obtained by simple stretching or incision of the hymeneal ring. Episiotomy is rarely indicated, and then need not be extensive. Approximately one-third of the patients in this series were nulliparas. We feel that a simple perineal incision, when necessary, will heal with less risk and discomfort to the patient than will an abdominal incision.

### Preoperative Preparation of the Patient

Hysterectomy is rarely an emergency operation. Sufficient time is usually available for adequate preoperative study and preparation of the patient. We believe that a considerable percentage of the postoperative complications which we have encountered in this series may have been due in part to a failure to complete fully such a study. We have previously referred to elimination of foci of infection as one of the prime requisites for good primary healing and uncomplicated convalescence after any operation. Distant foci, such as infected teeth, tonsils, sinuses, respiratory mucous membrane, or digestive tract can, we believe, be etiological factors in causing infections of the operative site which, because of trauma, is a point of lowered resistance. We feel that the same factors are the greatest cause of postoperative thrombophlebitis. In like manner we are convinced that proper healing is frequently interfered with by inadequate hemostasis or by disregarding pathogenic bacteria in the vagina. It would seem self-evident that an incision through a field that is infected is more dangerous than when the normal flora of the vagina is present. Far too frequently pelvic operations are undertaken in the presence of an unrecognized, nonvenereal type of vaginitis, such as trichomonas, monilia, or nonspecific infection, when the surgeon would not consider an operation in the presence of gonococci. We have conscientiously tried to check and eliminate all of these pathogenic conditions before operation. In reviewing our failures, we believe that many of the morbid postoperative conditions can be traced to our neglect to eliminate fully all possible foci of infection, or to obtain adequate hemostasis. Preoperative correction

many times the nature of an ovarian swelling can be determined preoperatively with a fair degree of certainty. The smaller benign ovarian cysts, such as follicular and chocolate cysts or dermoids, may be safely removed vaginally following hysterectomy. A posterior colpotomy as a preliminary step in hysterectomy will often disclose not only the nature of the adnexal swelling, but also the removability of the pathology in question. Direct observation of the lesion will determine the course of the subsequent procedure. In our series, previous pelvic or other abdominal surgery was not found to be as limiting as it seems to have been to other surgeons. In Group II, 34.3 per cent of the patients had had some form of previous abdominal surgery (Table I).

TABLE I. PREVIOUS ABDOMINAL SURGERY

GROUP II*	
TYPE OF OPERATION	NUMBER OF PATIENTS
Appendectomy	339
Cholecystectomy	53
Uterine suspension	24
Oophorectomy	18
Salpingectomy	14
Cesarean section	13
Herniorrhaphy	11
Laparotomy	10
Myomectomy	6
Nephrectomy	3
Gastric resection	2
Intestinal obstruction	1
	494
494 patients, or 34.3 per cent, in Group II had some form of previous abdominal surgery.	

\*Total for Group I not tabulated.

Uterine suspension was the third most common of these abdominal operations. Unfortunately, these figures for Group I were not tabulated. In general, any previous abdominal operation can complicate a hysterectomy from above as well as one from below. However, we feel that in many instances adhesions low in the pelvis were visualized and freed more easily through the vagina than would have been possible from above. In like manner, the adnexa are accessible to direct vision, and usually may be removed easily through the vaginal opening. In Group I, 247 patients had one or both ovaries removed, and 336 had unilateral or bilateral salpingectomy. In Group II the incidence was 91 and 81, respectively. Routine inspection of the adnexa is an integral part of vaginal extirpation of the uterus. We have had the opportunity to observe peritonealization following vaginal hysterectomy from the abdominal side in a few instances where an acute abdominal condition has necessitated a laparotomy during early convalescence, and in those few patients who came to autopsy. Peritonealization is adequate if the closing sutures are correctly placed. The most important sutures are those which secure the lateral corners of the vaginal cuff. These are introduced through the anterior vaginal mucosa, continued over the base of the bladder, through the peritoneum of the anterior cul-de-sac, thus obliterating dead spaces. With the same suture, the peritoneum is followed laterally to where the two leaves of the broad ligament have been divided. A running suture

Infection in postoperative hematomas, or conversely, delayed hemorrhage as the result of postoperative infection comprise a considerable proportion of the cases of morbidity. In view of these findings it would seem that meticulous hemostasis at the time of operation is much more important than the speed with which the operative procedure can be completed. Even the small vessels divided in the dissection of the bladder or incision of the vaginal mucous membrane when not secured, may result in considerable immediate external postoperative bleeding or large hematomas. When infection occurs in these areas, however, spontaneous drainage frequently takes place. Bleeding during operation can be lessened by the preliminary injection of oxytocics into the paracervical tissues. In the early cases in this study pituitrin was used; one patient, however, developed shock symptoms following the injection of pituitrin. This phenomenon has been adequately described by Simon<sup>15</sup> in 1935, and at that time pitocin was substituted for pituitrin, and no untoward symptoms have been observed since this change. We do not believe that the use of oxytocics predisposes to postoperative hemorrhage, since in this series this complication, when it occurred, was usually late in convalescence, from the fifth to the fifty-sixth day. This would probably indicate that the factors necessary for primary healing, such as good general nutrition, proper vitamin balance, and normal bleeding and coagulation time were lowered or interfered with by infection. When operative measures are undertaken for the control of this secondary hemorrhage, wide separation of the vaginal vault and general oozing from all areas are frequently present. No fatalities have occurred from this delayed postoperative bleeding.

Accidentally or purposely, in order to remove a tumor, usually endometriosis, involving the bladder base, the bladder has been opened a number of times. Immediate closure of the rent with interrupted sutures in layers and the insertion of a retention catheter to be retained for a week or ten days resulted in primary healing, except in five cases when a vesicovaginal fistula resulted. Three of the five resulting fistulae healed following the insertion of a radium needle. The other two cases were cured by secondary operative closure. There was one case of rectovaginal fistula in this series. It was the result of suturing for postoperative bleeding. To our knowledge nothing occurred in this series of cases either at the operation or afterward to suggest that we ever cut or ligated a ureter.

Prolapse of the Fallopian tube as a postoperative complication has been seized with avidity by many men who are opposed to vaginal hysterectomy. This occurred twenty-six times in Group I. Unfortunately, the figures for Group II were not tabulated. As Dr. Heaney<sup>2</sup> has explained in a previous article, "This accident is simply attended by making slight traction on the tube until it is completely delivered into the vagina, when a ligature is passed around the tubal mesentery and the tube burned off with a light nasal cautery. This generally requires no hospitalization. These patients suffered no more inconvenience than would be occasioned by the removal of excessive granulation tissue."

The average hospitalization for patients in Group I was 12 days, and in Group II was 13.5 days. The average for the last 72 patients in Group I was 10.8 days. This difference may be accounted for by improvement in technique,

of anemia, vitamin balance, and restoration to normal of blood protein which have been lowered by blood loss or poor nutrition are essential for resistance to infection and proper healing. Transfusions of whole blood or plasma preceding or during the operation are of equal or greater benefit to the patient's resistance than any ordinary antiseptic agent used in cleansing the vagina.

### Morbidity

The morbidity in this study has been calculated on the usual standard of morbidity for surgical patients, namely, a temperature of over 100.4° F. on any two consecutive days, excluding the first twenty-four hours. We thoroughly agree with Phillips<sup>13</sup> that this is not a true measure of gynecologic morbidity. On this basis, however, 66 per cent of Group I and 61 per cent of Group II were not morbid. In Group I, 34 per cent of the patients had a temperature of over 100.4° F. for one or more days, and 30 per cent of the patients in Group 2 had a temperature of over 100.4° F. for *no* more than two days. Thus, 91 per cent of the patients in Group II had a temperature of over 100.4° F. for *no* more than two days. We believe this illustrates an uncomplicated postoperative temperature curve for vaginal hysterectomy, since all of these patients had an otherwise uneventful convalescence. The statistics for morbidity in Group I were unfortunately not tabulated in group days. The findings above corroborate Jones and Doyle's<sup>14</sup> observations in their attempt to set up a temperature curve for normal convalescence in gynecologic surgery. On this basis we considered only 9 per cent of the patients in Group II to be truly morbid. However, adhering strictly to the usual standard of morbidity, 36.5 per cent, or 1,022, of the total 2,798 patients were morbid. This compares favorably with other morbidity studies of vaginal hysterectomy. We were able to recognize clinically the cause for morbidity in only 204 cases; therefore, we have subtracted this number from the total of 1,022, leaving 818 patients in whom the cause of the temperature elevation was undetermined. We have felt that these were most probably due to infections of varying degree in the operative site. The 9 per cent of the truly morbid patients usually gave definite evidence as to the cause of their prolonged fever, such as urinary tract infection, hematomas, or thrombophlebitis.

TABLE II. POSTOPERATIVE COMPLICATIONS

	GROUP I	GROUP II
Urinary tract infection	75	78
Postoperative bleeding, immediate or delayed	10	17
Pelvic abscess	2	8
Upper respiratory infection	1	7
Thrombophlebitis	1	3
*Intestinal obstruction	2	2
Pulmonary embolism	2	1
Cerebral embolism	0	1
Vesicovaginal fistula	2	3
Pituitrin shock	1	0
†Rectovaginal fistula	0	1
Prolapse of omentum into vaginal vault	1	0
Prolapse of ileum into vaginal vault	0	1
Parotitis	1	0
Prolapse of tube	26	-†

\*Two spontaneous recoveries, two deaths.

†Resulting from postoperative suturing for bleeding.

‡Not tabulated.



TABLE IV. PATHOLOGY AND ASSOCIATED CONDITIONS REQUIRING HYSTERECTOMY

	GROUP I	GROUP II
Fibromyomata uteri	859	765
Uncontrollable menorrhagia or metrorrhagia	452	686
Prolapsus uteri	118	271
Hyperplasia of endometrium	—*	145
Dysmenorrhea	70	39
Adenomyosis	204	213
Retroversion	16	17
Endometriosis	44	31
Postmenopausal bleeding	29	6
Cervical polyp	—	59
Endometrial polyp	—	50
Pelvic inflammatory disease	—	12
Cervical fibroid	1	1
Erosions	—	177
Ovarian cyst	24	4
Nabothian cyst	—	130
Pregnancy	—	10
Dermoid cyst	10	4
Fibroma of the ovary	3	3
Brenner tumor	1	0
Stricture of the cervix (previous amputation)	23	—
Sterilization procedure	11	—
Bladder tumor	1	0
Previous interposition operation with bladder symptoms	3	0
Chocolate cyst	5	3
Chorionepithelioma	—*	2†
Persistent leucorrhea uterine in origin-postirradiation	17	1
Tubal pregnancy	2	1

\*Not tabulated.

†One questionable diagnosis.

### Mortality

The criteria by which any operative procedure should be judged are safety, effectiveness, and comfort to the patient. From a summation of the preceding data, it would seem that vaginal hysterectomy more completely fulfills the above criteria than do total or subtotal abdominal hysterectomy. We believe the various symptom-complexes of pelvic disease can be more effectively treated and completely relieved by vaginal than by abdominal surgery. We and our patients are convinced that, in general, vaginal surgery is less painful than is abdominal surgery. Abdominal hysterectomy in our hands has had approximately six times the mortality rate of vaginal hysterectomy. It is true that, when we cannot remove a uterus vaginally and must resort to the abdominal route, that case is often more serious than the average of the cases that we operate upon vaginally. However, this by no means explains the difference in mortality. We wish to emphasize that we do not reserve for abdominal operation the serious cases and operate vaginally only the simple ones. The determining factor to operate abdominally rather than vaginally was only occasionally that the uterus could not be removed vaginally. Usually the deciding factor was much simpler—a very large fibroid in a woman with a narrow vagina, bilateral ovarian cysts where the hysterectomy was coincidental, malignancy of the ovaries where hysterectomy was a necessary accompaniment, were some of the frequent indications for the choice of the abdominal route. The great difference in mortality

the increased tendency toward early dismissal from the hospital or, since the number is small, it may not have included as many postoperative complications or as many extensive repairs, both of which conditions naturally lengthen the hospital stay and increase the chances of morbidity. The average stay for the 391 patients in Group II who had vaginal hysterectomy alone was 10.9 days.

A tabulation of additional operative procedures performed in these two groups is shown in Table III. This comparison illustrates not only the large number of associated lesions which can be adequately and safely treated per vaginam, but also indicates that as improvement in operative skill develops, more and more associated pathology can be corrected vaginally. Of the entire series, 2,098 patients, or 75 per cent, required additional surgery beyond that of simple vaginal hysterectomy.

TABLE III. ADDITIONAL SURGERY

	GROUP I	GROUP II
Posterior colpoperineorrhaphy	719	895
Anterior colporrhaphy	108	269
Urethroplasty	160	249
One or both ovaries removed	247	91
One or both tubes removed	336	81
Resection of endometrial transplants	—*	5
Removal of Bartholin cyst	10	3
Ventral herniorrhaphy	1	2
Removal of adenoma of the rectovaginal septum	14	—
Vulvectomy	5	—
Hemorrhoidectomy	10	—
Repair of rectovaginal fistula	1	—
Removal of mucoid cyst of colon	1	—
Repair of complete perineal tear	4	—

\*Not tabulated.

The gross and microscopic pathology are shown in Table IV.

Listed in this table are some conditions, such as menorrhagia, metrorrhagia, retroversion, etc., which were only a part of a complex clinical picture. Alone, many of these conditions are not indications for removing the uterus, but when taken in combination with one or more other factors, they seem to indicate hysterectomy as the surest and safest way of curing all of the patient's symptoms with one operative procedure. The majority of the cases listed under uncontrollable menorrhagia, metrorrhagia, retroversion, and dysmenorrhea had previously had the benefit of the more conservative medical and surgical treatments without adequate relief. Six of the ten cases listed under pregnancy were performed on patients where hysterectomy had been advised, but the operation was delayed until they were pregnant in an attempt to get early ova for study. The remaining cases of pregnancy were either unsuspected, or the uterus was removed as a part of a therapeutic abortion and sterilization procedure. We all believe that, since hysterectomy is the surest method of sterilization, it is the method of choice when gross uterine pathology or marked disturbances in pelvic physiology is present, especially in older patients, particularly when in addition there is considerable relaxation of the pelvic floor to repair. The Brenner tumor and the bladder tumor were conditions found in addition to the pathology indicating vaginal hysterectomy.

The mortality for these 2,798 vaginal hysterectomies was six deaths, or 0.214 per cent (Table V). These six deaths were equally divided between the two groups, three deaths occurring in each group. In Group I, those done by Heaney, 745 hysterectomies have been done since the last death.

Statistical study of the literature reveals an approximate comparison. The average mortality for abdominal hysterectomy, both total and subtotal, in 40,587 cases collected from the literature was 1,019 deaths, or 2.5 per cent (Table VI).

Only 18 deaths were reported in 4,482 vaginal hysterectomies, or 0.40 per cent (Table VII). The average rate for the entire series with our groups included is abdominal, 2.4 per cent; and vaginal, 0.32 per cent.

### Summary

1. Two thousand seven hundred ninety-eight vaginal hysterectomies and 898 abdominal hysterectomies are reported, and the mortality is compared with 4,482 vaginal and 40,587 abdominal cases reported in the literature.

2. The mortality rate of the collected cases of abdominal hysterectomies is 7.5 times greater than that of vaginal hysterectomies.

3. Therefore, vaginal hysterectomy should be chosen whenever feasible because: (a) It permits a more regular correction of all defects than do other procedures. (b) The vaginal route causes less discomfort to the patient. (c) No abdominal scar is produced. (d) Pulmonary complications and emboli are less frequent. (e) Thrombophlebitis and pelvic abscess are less common. (f) Trauma to the bowel, postoperative adhesions, ileus and bowel obstruction are infrequent. (g) Gas pains are less severe. (h) It is less radical and safer than irradiation. (i) It affords a safe approach to many forms of adnexal pathology. (j) Peritonealization can be accomplished as accurately as by the abdominal route. (k) Stump carcinoma and persistent cervical discharge are prevented.

4. We agree with many who have advocated vaginal hysterectomy rather than abdominal hysterectomy in poor operative risks. It then seems logical that vaginal hysterectomy is an even safer procedure in patients who are in better operative condition.

5. Previous abdominal surgery need not always contraindicate vaginal removal of the uterus.

6. The technical skill of the operator is of no greater importance than is the choice of method of approach or preoperative preparation of the patient, such as: (a) eradication of foci of infection; (b) correction of anemia, vitamin, protein and fluid balance; (c) restoration of the normal vaginal flora.

7. Meticulous hemostasis is vitally important.

8. Adequate training in vaginal hysterectomy will equip a surgeon with the confidence and ability to treat many other gynecologic conditions by vaginal surgery to the great benefit of the patient.

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between vaginal and abdominal hysterectomy can be explained on no other basis in general than the inherent risks between the two methods of approach.

Our mortality rate in 898 abdominal hysterectomies during approximately the same interval by the same group of surgeons was 10 deaths, or 1.22 per cent.

TABLE V. CAUSES OF DEATH

	AGE	OPERATION	DIED	CAUSE
*1.	Mrs. M. Z.	40 Vaginal hysterectomy and posterior colpoperineorrhaphy	7th post-operative day	Peritonitis
2.	Mrs. B. C.	38 Vaginal hysterectomy, left oophorectomy	5th post-operative day	Intestinal obstruction
*3.	Mrs. A. C.	60 Vaginal hysterectomy, anterior colporrhaphy, urethroplasty, posterior colpoperineorrhaphy	18th post-operative day	Thrombophlebitis, pulmonary embolism, hypertensive heart disease.
*4.	Mrs. G. E.	34 Vaginal hysterectomy	6th post-operative day	Intestinal obstruction acute myocarditis
5.	Mrs. A. S.	49 Vaginal hysterectomy, posterior colpoperineorrhaphy	Day of operation	Hemorrhage
*6.	Mrs. F. Z.	45 Vaginal hysterectomy, right salpingo-oophorectomy, posterior colpoperineorrhaphy	31st post-operative day	Peritonitis, pelvic abscess, spontaneous drainage

\*Autopsy.

NOTE.—Cases 1, 2, and 3 were in Group I. Cases 4, 5, and 6 were in Group II.

TABLE VI. ABDOMINAL HYSTERECTOMIES: TOTAL AND SUBTOTAL

AUTHOR	NUMBER	DEATHS
Smith <sup>4</sup>	837	6
Miller and Prejean <sup>16</sup>	629	12
King <sup>17</sup>	537	5
Williams <sup>18</sup>	1,870	52
Mengert <sup>19</sup>	1,925	38
Bryan and Trabue <sup>20</sup>	29,442	849
McDonald <sup>21</sup>	2,628	27
Masson <sup>10</sup>	2,184	21
Dannreuther <sup>22</sup>	535	9
	40,587	1,019=2.5%
Campbell	898	10
	41,485	1,029=2.4%

TABLE VII. VAGINAL HYSTERECTOMIES

AUTHOR	NUMBER	DEATHS
Danforth <sup>23</sup>	517	0
Tyrone and Weed <sup>24</sup>	305	2
Wagh <sup>5</sup>	600	2
Averett <sup>11</sup>	934	3
Babcock <sup>12</sup>	300	0
Tofer <sup>25</sup>	210	0
Burwig <sup>26</sup>	100	1
Masson <sup>10</sup>	782	6
Miller and Prejean <sup>16</sup>	199	2
Smith <sup>4</sup>	363	0
Phillips <sup>13</sup>	84	1
	4,482	18-0.40%
Campbell	2,798	6
	7,280	24-0.32%

ample time elapses between time that a decision to operate is reached and the time the patient is admitted to the hospital for almost any corrective procedure.

We also agree that removal of the uterus, whether vaginally or abdominally, does not shorten the vagina, but regardless of the type of procedure, the vagina will be shortened if cyst-rectocele prolapses and enterocele are present. In many instances, the vagina is congenitally shortened before any of these pathologic conditions develop.

We do not want to be seemingly annoyingly persistent in this question of morbidity—we have presented remarks concerning this subject from this forum. Here is an excellent opportunity for the establishment of a norm-curve for vaginal hysterectomy. Certainly the comparison of these temperature curves to 100.4° F. for 48 hours is ridiculous.

Table III shows an increase in the percentage of patients who have had, in addition to vaginal hysterectomy, other reparative operations. We believe in almost every instance of vaginal hysterectomy in multiparous women that repair of the anterior and posterior vaginal walls should be done.

In Table IV, which deals with direct and associate pathology, significant figures appear; a few we repeat: menorrhagia and metrorrhagia, 686; hyperplasia of endometriosis, 145; erosions, 177; nabothian cysts, 130. We realize that these conditions represent in many instances the associate pathology in the same patient, but it emphasizes, however, that these patients are being treated by some reparative procedure which conserves the uterus. To this we subscribe wholeheartedly.

Again we commend the authors for their meticulous study of a very interesting group of patients, well treated and with enviable results.

DR. RALPH A. REIS.—We owe Dr. Heaney gratitude for gradually widening the indications for vaginal hysterectomy, for developing a superb technique, and for the Heaney clamp which has made vaginal hysterectomy a simpler operation. But I think that he and his group have been overenthusiastic.

I believe that the vaginal approach and the abdominal approach should be in no way competitive. Each method has its own indications and contraindications. If this were not so, the essayist would not be able to present 800 abdominal hysterectomies done during the time that 2,800 vaginal hysterectomies were performed. He stresses a proper choice of methods and then goes out wholeheartedly for vaginal hysterectomy alone. He does not have a choice when he has a preconceived notion that vaginal hysterectomy is the method of choice and is the safest way to do a hysterectomy. Under Dr. Campbell's list, the contraindications are, endometriosis, chronic pelvic infection, diverticulitis of the colon, and ovarian tumors associated with uterine pathology. It is amazing to me that only 12 patients out of some 2,900 should have some evidence of pelvic inflammatory disease. That is not true in the service at Michael Reese. Perhaps we did not screen the patients so as to avoid doing vaginal hysterectomy on those having pelvic inflammatory disease. At the present time we find we meet with this condition frequently and often inadvertently.

I am not enthusiastic for radium, but I would deny that vaginal hysterectomy carries a lower mortality than a so-called menopausal dose of radium, although the end results are less satisfactory.

I agree that previous abdominal surgery is no contraindication, particularly when 34.3 per cent of 494 patients had had some form of previous abdominal surgery. Breaking down these figures, we find that 28.2 were appendectomies, cholecystectomies, nephrectomies, and gastric resections. That type of abdominal surgery does not interfere with vaginal surgery. Only 6 per cent of the patients had had previous pelvic surgery. But previous pelvic surgery is not a contraindication for vaginal hysterectomy except in a few specific instances.

Vaginal hysterectomy is not an emergency operation, but I do contend that it is often an urgent operation. From Dr. Campbell's figures, more than half of the patients were operated upon for vaginal bleeding. Vaginal bleeding to my mind constitutes an urgent need for surgery. To permit bleeding for weeks and months while removing foci of infection in the way of teeth, tonsils, and sinuses is not helpful. It is an error in clinical judgment as are the other recommendations in preoperative care. I do not know how to restore the normal

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### Discussion

DR. HAROLD O. JONES.—This very large series of operations so reduces the mathematical percentage of error that a true picture of results is obtained. We are all grateful to Dr. Heaney and his associates for the stimulation we have received from frequent reports of the results obtained in this type of operation.

We disagree with the essayist in his differentiation of "ability to decide the type of operation" from "the technical skill and manual dexterity of the surgeon." We believe these factors go hand in hand and improve as experience expands. Reduction in mortality and morbidity reflects increased experience. Careful supervision and training are responsible for the excellent showing of the resident staff.

Our experience has been that it is best to begin to teach others the technique of vaginal hysterectomy in patients with some relaxation and proceeding to other combinations of associate pathology as experience broadens. We must never forget that, for the average, this is a fairly difficult technical operation and must not be made to appear too simple. We must not forget that this society, in its discussions and clinics, sets a standard of accepted thought and technical procedures. This carries additional responsibilities.

As Campbell has said, if the uterus should be removed the vaginal route is preferable, if possible. With this we agree. All favorable factors are certainly true, and especially phlebitis and embolism. In a smaller series of our own we have not had an instance of phlebitis or pulmonary embolism. I am not so sure, however, of the exact reasons for this favorable phase.

All the indications offered for this type of operation are sound. We wish to join with the author in condemnation of the use of radium in benign uterine diseases as a substitute for hysterectomy. We have one additional observation which applies to results obtained by various plastic procedures without hysterectomy. In reviewing our own cases we have been impressed by the superior results obtained in similar conditions treated by vaginal hysterectomy.

The preoperative treatment outlined is especially thorough, and we are glad the author called attention to reduction of blood protein in many of these patients, quite certainly an important factor in recovery after operation. We are all well aware of the fact that now

The question I would like to ask the essayist is, do you consider vaginal hysterectomy the treatment for what I call herniation or what you see fit to call prolapse of the uterus? If it is prolapse of the uterus, what do you do with the rest of it, because that is not all of the pathology. If there is herniation of the uterus, there is herniation of a lot of other structures. What do you do with those hernias? I do not consider that vaginal hysterectomy is the treatment for herniation. It may go with the herniation and other things for which the uterus should be taken out. You do vaginal hysterectomy for pathology that is in the uterus. You cannot do vaginal hysterectomy for pathology that is left in. That is not the treatment for herniation.

DR. CHARLES E. GALLOWAY.—I have some questions that we might ask about this series of 2,700 vaginal hysterectomies. There has been no mention made of the discovery of any early cervical carcinomas. I realize that this series is on benign cases, but it seems to me we remove a uterus now and then in which we discover an early carcinoma. Were such discoveries made?

Also, we find that anemia is a common condition following vaginal hysterectomy, more so than following abdominal hysterectomy. Postoperative anemias are sometimes quite severe. We think this operation requires a man to move quite rapidly because of the fact that back bleeding occurs from unclamped vessels in the opposite side of the uterus as it is being removed.

Moreover, the time required to remove the uterus through the vagina is a factor to consider. In our hands the ordinary vaginal hysterectomy requires seventy-two minutes, and, where we do a repair also, it takes about eighty-five minutes. These figures are much larger than those for abdominal hysterectomy.

Our ratio of abdominal to vaginal hysterectomy is 2.6 to 1. Over the last five years we had 298 vaginal, 521 total abdominal, and 255 subtotal abdominal hysterectomies. I would also like to know if any cases out of this 2,700 had a prolapse of the vagina later on.

DR. CAMPBELL (Closing).—We, as you know, have been accused at Presbyterian Hospital of doing too many vaginal hysterectomies, but we still feel that it is the method of choice whenever it is feasible, as I think the paper indicated. The original idea in trying to present this paper was that many men, as I understand from the older members of the Society, have remarked so frequently that it was perfectly fine for Dr. Heaney to do vaginal hysterectomies because he is a wonderful technician and very skilled with his hands, but that the rest of us could not do it as well. We feel that possibly one of the reasons we are able to present the results we did is, as one of the discussors said, we have been trained by the master. This is probably true, but we are still trying to train other men who will also be teachers and will teach this method which we believe our figures show is the safer procedure in the majority of cases.

Dr. Jones said they like to start their residents off with vaginal hysterectomies associated with some relaxation. This is certainly a debatable point. We still feel that most hysterectomies are easier when there is no appreciable relaxation; the more or less difficult part is that the lateral walls of the vagina fall together and obliterate the field. We agree with Dr. Jones in his statement that we do not advocate this as a cure-all or procedure to be done by the man who does not have training in vaginal surgery.

I am unable to answer Dr. Reis as to why we did not find more pelvic inflammatory disease. All I know is what the record showed.

Dr. Barrett suggested that perhaps we are advocating vaginal hysterectomy as a cure-all. I can assure him we do other things at Presbyterian Hospital besides vaginal hysterectomy. I am sorry about the use of the word prolapse.

Dr. Galloway asked about carcinoma of the cervix and of the body. We do those cases, but, as you mentioned yourself, the paper was written on vaginal hysterectomy for

vaginal flora. I have a great number of patients in whom I cannot get rid of *Trichomonas*. I have yet to learn how to restore vitamin balance. I do think that his one statement concerning preoperative preparation which is most important is that we use liberal and repeated blood transfusions.

Finally, I believe we should not compare mortalities by the abdominal and the vaginal method. He states that the mortality by the abdominal approach is six times more than it is by the vaginal approach. I deny the fundamental principle that all hysterectomies should be done vaginally, which even Dr. Campbell admits is wrong because he states that 800 out of 3,600 were done abdominally. If only the simpler ones were done vaginally and the so-called difficult ones were done abdominally, then certainly the comparison is erroneous. Finally, if our group at Michael Reese showed seven times as much mortality following abdominal hysterectomy as follows vaginal hysterectomy, I would suggest that we stop doing vaginal hysterectomy and do only abdominal hysterectomies to learn how to attain a safer and more comparable mortality.

DR. EDWARD ALLEN.—When Dr. Heaney found he could not come from California for this meeting, he sent me the following discussion of the paper. Dr. Heaney said:

"I am very glad that this paper was written, and I take a great deal of personal pride in this study. It is conceivable that one man might lie about his results in order to bolster his reputation, but it is hardly believable that the whole staff of a reputable hospital would do so.

"The papers that I have presented on vaginal hysterectomy have met with a good deal of skepticism; in some instances, I have been accused of falsifying the reports or at least have failed properly to emphasize the bad results obtained. However, in all the papers, as well as this one, every detail of importance has been given, and an honest attempt has been made to set before the profession all the known facts.

"This paper presents the largest collection of vaginal hysterectomies with the lowest mortality when the number of cases reported is taken into consideration. It will be noted that I personally performed 745 vaginal hysterectomies since the death of the last patient, which is the largest number of cases reported without fatality.

"I wish, however, to state that from now on, in the hands of careful operators, our record read to you tonight should be easily surpassed in the future.

"The six deaths reported in this paper all occurred, or largely so, at least, before the use of chemotherapy and antibiotics. Two of the deaths were due to peritonitis, which might well have been prevented by the use of sulfonamides and penicillin. One death was due to a pulmonary embolus secondary to a thrombophlebitis, underlying which was an inflammation. Two cases were due to intestinal obstruction, of which an inflammation might well have been the cause. One death was due to hemorrhage, the only death which would not have been modified by the present-day therapy, so it is quite probable that in the future large series of vaginal hysterectomies may be reported without a single fatality."

DR. CHANNING W. BARRETT.—I have looked upon my work with the idea that there are a lot of things to be done for a woman besides vaginal hysterectomy. I started many years ago with the idea that vaginal hysterectomy had many advantages, but I never got away from the idea that it was not applicable to all cases. There are as many cases in which the indications are for abdominal hysterectomy as for vaginal hysterectomy, and I do not think we should let the idea go forth that vaginal hysterectomy is superior in all cases. It is not a simple operation, not as simple as the essayist made it appear. Heaney does a wonderfully safe vaginal hysterectomy. He does vaginal hysterectomy that I have seen that certainly should have been done abdominally. We will not go into the question of what is the indication for one and what is the indication for the other, but I would like to call attention to the fact that they speak of these vaginal hysterectomies for "prolapse." These are prolapses, they are hernias. There is much talk of prolapse and relaxation where the condition is one pelvic floor injury and resulting herniation. What did the condition come from? Stress and strain. If the woman has had stress and strain until she has no pelvic floor and no musculofascial structure, would the diagnosis of relaxation be correct? It is not relaxation, it is a hernia, with the absence of any musculofascial floor.



## ARRHENOBLASTOMA OF THE OVARY, WITH A REPORT OF TWO CASES

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TWO patients with arrhenoblastoma of the ovary have recently been studied in the Gynecological Department of the Johns Hopkins Hospital. Because of the extreme rarity of the condition and the paucity of 17-ketosteroid determinations on such cases, they were considered worthy of reporting in some detail.

CASE 1.—J.H.H. No. 337531. Mrs. S. F., white, aged 36 years, a private patient of Dr. Leo Brady, was first seen in November, 1944, complaining of vaginal spotting every two weeks. When 15 years of age she had noticed a fine growth of hair on the upper lip, chin, and cheeks. At about the same time her breasts began to develop, and, although this development continued normally, no menses appeared. At the age of 18 years menstruation finally began, but the interval was irregular and prolonged, varying from three to six months. The flow was scant in amount and lasted only one to two days. After marriage, at the age of 23 years, the menstrual interval decreased somewhat and varied from one to three months, but the amount and duration of the flow remained unchanged. She never became pregnant, although she never practiced contraception.

Two months before her first hospital admission slight vaginal bleeding had begun to occur about every two weeks. Because of this a dilatation and curettage was performed on Nov. 6, 1944. On examination under anesthesia it was thought that the uterus contained a small myoma. Microscopic examination of the curettings revealed early proliferative endometrium.

The spotting continued at intervals of about two weeks until April, 1945, when the menses ceased entirely. She was readmitted to the hospital on Aug. 2, 1945, and at this time physical examination showed a somewhat obese woman, 5 ft. 2¾ inches in height and weighing 165 pounds. The obesity was limited to the trunk, the arms and legs being relatively small and muscular with exceptionally well-developed gastrocnemius and quadriceps femoris muscles. There was hypertrichosis of the cheeks, lips, chin, and chest, distinct masculine distribution of the abdominal and pubic hair, and marked hypertrichosis of the lower back, buttocks, and thighs. The breasts were well developed and pendulous in type. The general physical findings were essentially negative except for a blood pressure of 176/96. On abdominal examination, an ill-defined mass could be felt in the left lower quadrant. On pelvic examination the labia majora were found to be small and the labia minora almost absent. The clitoris was not enlarged and there was no abnormality of Bartholin's or Skene's glands. The cervix was normal in size, consistency, and appearance, and pointed posteriorly. The body of the uterus was small and displaced anteriorly and toward the left by a mass in the right adnexal region. It was apparently the displaced body of the uterus which had been felt abdominally. The adnexal mass, which was about 9 cm. in diameter and irregular in contour, was freely movable, and apparently replaced the right ovary. The left ovary seemed slightly enlarged.

At operation on Aug. 3, 1945, the uterus, tubes, and left ovary appeared normal. The right ovary was replaced by a solid tumor 9 cm. in diameter. The

benign disease of the uterus. As I recall the figures, Dr. Heaney had 77 cases of carcinoma in his 1,300 cases. I do not know what the percentage was of the cervix and of the body. In our group there were roughly 40 in which hysterectomy was done in the presence of carcinoma of the cervix or body. That would have brought out much more discussion from the floor had it been in the paper. We did not evaluate the difference in the time necessary to do a vaginal hysterectomy alone or one with additional procedures. In trying to train our residents, as stated in the paper, we do not believe that the time element is very important. Much more important is meticulous hemostasis.

I did not have any figures for anemia following vaginal hysterectomy. I do not believe that has been a complication in our series of patients. Whether or not, again, it is due to careful hemostasis, I do not know, but we are very particular in ligating small vessels.

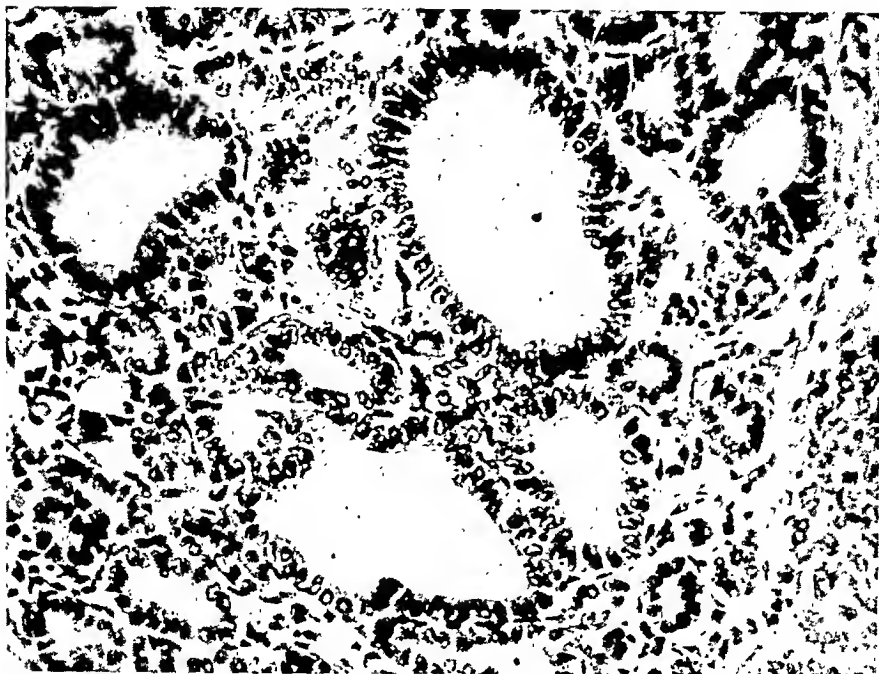


Fig. 2.—Gyn. Path. No. 63028. High-power photomicrograph of tumor from patient in Case 1, showing extremely well-developed tubules. No interstitial cells are present.

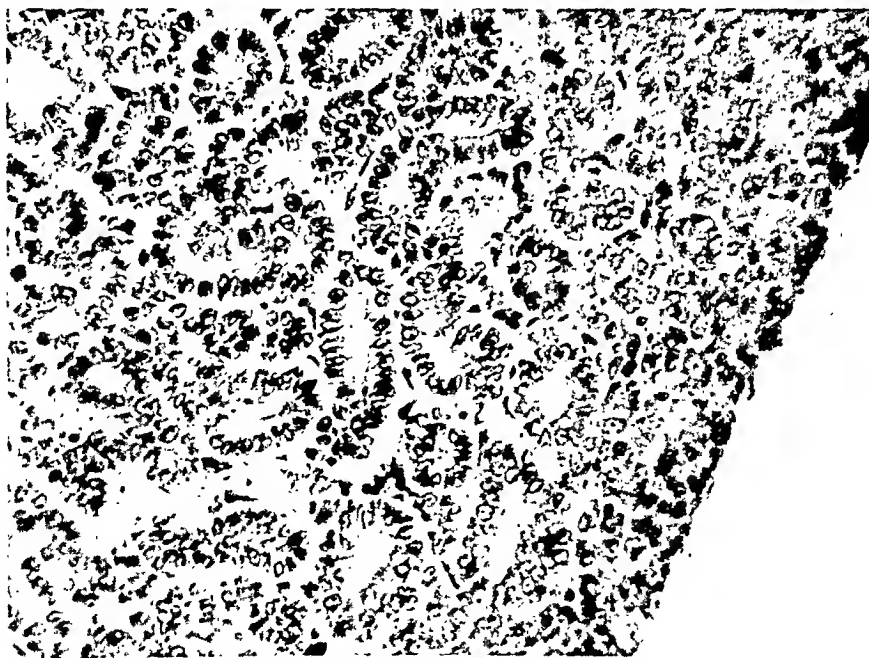


Fig. 3.—High-power photomicrograph from same tumor as Fig. 2, showing tubular development but also occasional interstitial cells, represented by the small dark-staining cells; these are deeply eosinophilic.

surface of the tumor was grossly corrugated and of a purplish brown color. There was no evidence of peritoneal metastases or implants, and exploration of the liver and retroperitoneal lymph nodes failed to reveal metastatic growth. The uterus, including the cervix, and both tubes and ovaries were removed. The patient made an uneventful recovery and was discharged on the sixteenth post-operative day. When last seen six months after operation, she was well with no evidence of recurrence.

The pathologic examination showed a normal uterus and patent tubes. The right ovary was completely replaced by a tumor measuring 11 by 8 by 8 cm. The tumor was apparently solid and well encapsulated with a smooth surface. It was yellowish gray in color, except for a small nodule on the posterior surface which was bluish and hemorrhagic. On section the tissue had a rubbery consistency and was separated into lobules by white, fibrous appearing trabeculae (Fig. 1). The left ovary measured 5 by 3 by 2 cm., and was apparently normal.



Fig. 1.—Specimen removed from patient in Case 1, showing appearance of cut surface of right arrhenoblastoma. The uterus has been opened.

Microscopically, the tumor was composed almost entirely of well-differentiated tubular elements (Figs. 2 and 3). It was necessary to search through several low-power fields before discovering any interstitial cell elements, and these then were frequently represented by single cells; such cells were easily recognized by the deeply eosin staining cytoplasm. Certain areas of the tumor might have been mistaken for a microfollicular granulosa-cell tumor.

In reviewing this case, it seems to be an arrhenoblastoma associated with relatively few masculinizing tendencies. The patient's symptoms of sexual maldevelopment, such as hirsutism, irregular menses, and sterility, date from puberty, and possibly indicate a congenital abnormality of the sex ridge with much later tumor formation. The symptoms which we believe were associated with the development of the tumor began just one year before her operation and consisted of an interruption of any menstrual rhythmicity, constant spotty bleeding, and finally, complete amenorrhea. A review of the literature shows that it is not uncommon for a patient with arrhenoblastoma to have a period of functional bleeding before developing amenorrhea; this was indeed the case in both of our patients. On physical examination the patient showed no enlargement of the clitoris which was present in our other case and is a very constant finding in those cases reported in the literature. It would seem that the paucity of masculinizing symptoms associated with the tumor growth is directly related

On physical examination the patient presented the appearance of a healthy young woman with normal feminine body configuration. There was a moderate amount of coarse hair on the arms, legs, and especially the face, and a small amount of pubic hair extended up to the umbilicus. The breasts were normally developed and revealed no abnormal masses and no secretion. Examination of the heart, lungs, and abdomen revealed normal findings. Scalp hair did not recede and there was no bald spot. No acne was noticed.

Pelvic examination showed normal external genitals, except for the clitoris which was definitely enlarged, being about 2 cm. long by 1.5 cm. in diameter. The outlet was marital. There was no bleeding or abnormal discharge. There was no enlargement of Bartholin's or Skene's glands. The cervix felt normal and appeared normal on speculum examination. The uterus was normal in size and in excellent anteversion. The right ovary was about two and a half times normal size, quite firm, and freely movable. The left ovary seemed a little smaller than average. Rectal examination was merely confirmatory of the vaginal palpation.



Fig. 5.—Cut surface of tumor from patient in Case 2.

The presumptive diagnosis was arrhenoblastoma of the right ovary, and the patient was admitted to the hospital on Dec. 26, 1944, where the following studies were carried out:

The hemoglobin was 14.5 Gm., and the Wassermann reaction was negative. The basal metabolic rate was plus 15 per cent, with a blood cholesterol of 227 mg. per cent. The serum chlorides were 142 meq.; blood chlorides, 99 meq.; carbon dioxide combining power, 30 meq.; and the blood sugar 78 mg. per 100 c.c. The results of a glucose tolerance test are shown in Table I. A urinary pregnanediol determination on a 48-hour specimen showed no pregnanediol to be present. Seventeen-ketosteroid examinations on two 24-hour urine specimens preoperatively showed 56 and 36 mg. per 24 hours.

Operation was performed on Jan. 2, 1945. Through a lower midline incision the pelvis was explored. The uterus and tubes were normal. The left ovary was slightly smaller than average and adherent posteriorly to the broad

to the scarcity of the interstitial cell elements of the tumor as seen on microscopic examination. This fact has been found to be generally true among the Pick type of tumors.

CASE 2.—J. H. H. No. 340274. Mrs. C. B., White, aged 26 years, first consulted us on Dec. 18, 1944, complaining of menstrual irregularity of three years' duration. In the past her general health had been good, typhoid fever at the age of 9 years had been her only serious illness, and she had experienced no accidents or surgical operations. The menses had begun at 12 years of age, and until the onset of the present trouble had always been regular and painless, with an interval of about twenty-eight days, duration of four days, and average amount of flow. She had had occasional slight leucorrhea, but had never experienced urinary or digestive symptoms. She had been married two and a half years, but had not become pregnant.

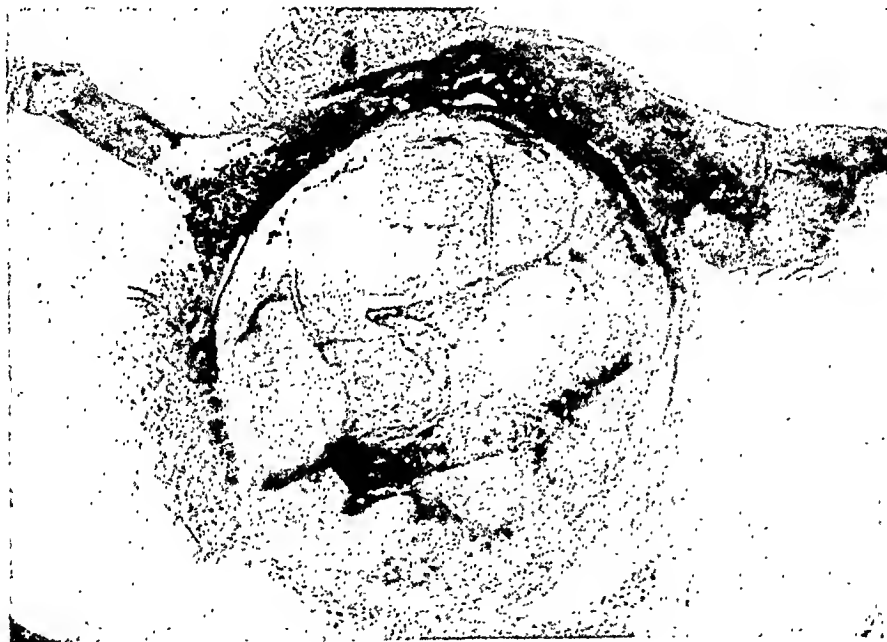


Fig. 4.—Specimen removed from patient in Case 2. Right ovarian tumor and tube.

In the patient's opinion, the onset of the condition for which she consulted us was attributed to the giving of two transfusions at an interval of only about a week three years previously. Soon after this the menstrual interval decreased to two weeks, and the duration of the flow at first increased to six days and then gradually to as long as thirteen days. She then began "to take shots" and missed first one period and then, after one normal flow, experienced amenorrhea for ten months. Following this she menstruated regularly and normally for three months, following which amenorrhea recurred and persisted for five months until she consulted us. At the onset of the menorrhagia three years previously the basal metabolic rate had been determined and she had been given thyroid extract, but she had no accurate knowledge as to the result of the metabolism test or the dosage of thyroid.

In talking with the patient, it was observable that the voice was slightly husky and that there was a little more than normal feminine facial hirsutism. The thought occurred to us that the "shots" might have been androgenic therapy, but upon careful questioning it was found that she had observed the voice change and increase in hair and was quite certain that they had antedated the "shots."

TABLE I

TIME	BLOOD SUGAR	URINE SUGAR
1½ hr.	150 mg.	0
1 hr.	75 mg.	0
2 hr.	55 mg.	0
3 hr.	73 mg.	0

salpingo-oophorectomy was done, after which the right round ligament was plicated over the area of cornual excision, and the appendix was removed.

The specimen consisted of a tube 8 cm. long which had a patent lumen and appeared to be normal. The ovary measured 3 by 3 by 4.5 cm., and was almost completely replaced by tumor. Grossly, the tumor appeared to be cystic, as it was bluish, glistening, and translucent (Fig. 4). On section, however, it was found to be a solid, well-encapsulated tumor of soft consistency with a mottled surface of yellow and reddish areas (Fig. 5). Microscopically, the tumor was composed almost entirely of interstitial cell elements; large masses of cells with eosin-staining cytoplasm and small hyperchromatic nuclei (Figs. 6 and 7). These cell masses were interspersed with areas of small spindle cells which, in certain areas of the tumor, could be seen to differentiate into tubular-like structures. Because of the relatively poor development of the tubular elements in the tumor, it has been classified as an arrhenoblastoma of the intermediate cell type.

The patient made an uneventful recovery. Urinary pregnanediol and 17-ketosteroid determinations were repeated twelve days postoperatively. The pregnanediol value remained 0 mg. per 24 hours, while the 17-ketosteroid level had fallen to 11 mg. per 24 hours.

She returned for her first follow-up visit on March 6, 1945. At this time she seemed to be in excellent health, and reported that she had had a period beginning January 28 which lasted four days, and was in every way normal except for cramps which she had not usually experienced. A second normal period had begun on February 21. There had been no regression in the hirsutism or change in the voice, but the clitoris, though still larger than normal, was definitely smaller than before operation.

The patient was last seen on Oct. 31, 1945. There was still no improvement in the hirsutism or voice, but the clitoris was only about 1 cm. in length and 7 or 8 mm. in diameter. Since her previous visit she had continued to menstruate fairly regularly, with an interval of 22 to 27 days and duration of four to five days. Since the period in January there had been no further pain.

### Comment

The two cases of arrhenoblastoma of the ovary here reported presented quite different pathologic appearances and clinical histories. Case 1 had very little evidence of masculinization, except for considerable hirsutism and rather marked muscular development, symptoms which had persisted over a period of sixteen years. Complete amenorrhea had been present for a period of eight months, and this seemed to be the only symptom associated with the tumor which she was known to have had for at least a year. The microscopic picture of this tumor fitted well with the clinical findings as it was predominantly tubular, closely resembling the tubular adenoma type of Pick.

The second case had a rather acute onset of symptoms which had progressed over a three-year period. Masculinization was definite, including hirsutism, hoarseness, and enlargement of the clitoris. Amenorrhea was also present. The urinary output of 17-ketosteroids was 56 and 36 mg. per 24 hours on two different days preoperatively. Twelve days postoperatively the level had fallen to 11 mg. per 24 hours, which is within the normal range. The microscopic ap-



ligament by filmy adhesions which were easily freed. Otherwise this ovary appeared normal. The right ovary was converted into a small spherical tumor about 5 cm. in diameter, which was also adherent to the posterior surface of the broad ligament by filmy adhesions. When these adhesions were released and the tumor brought forward, it superficially appeared to be cystic, but this appearance was found to be due to several small cysts near the surface. A right

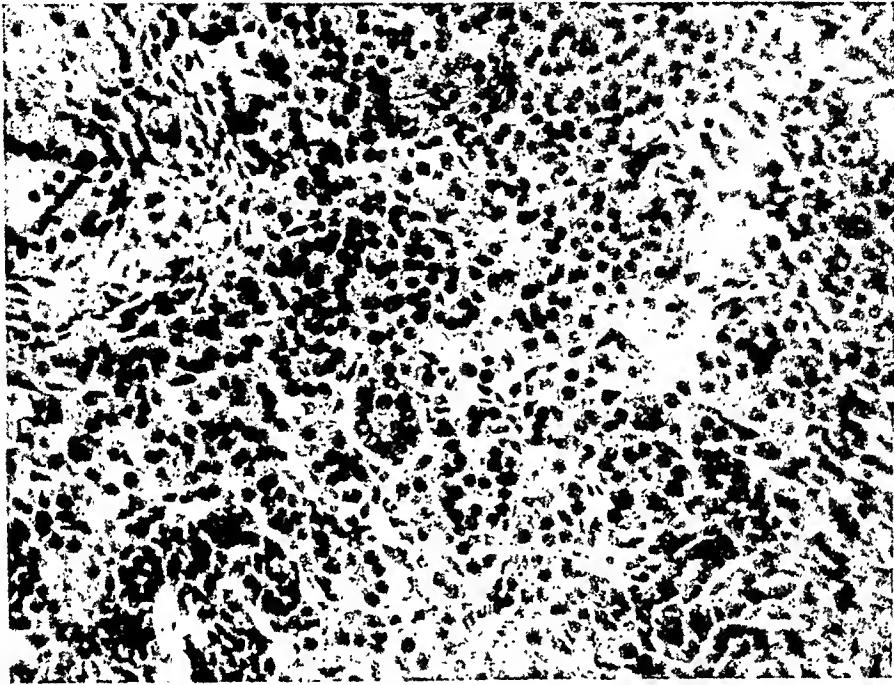


Fig. 6.—Gyn. Path. No. 61222. High-power photomicrograph of tumor from patient in Case 2 showing masses of interstitial cells.

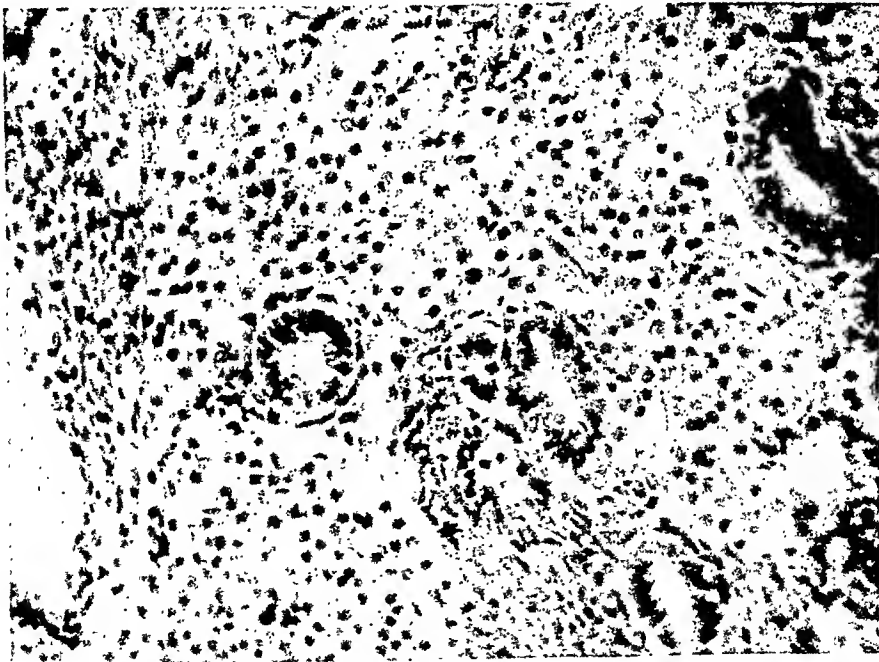


Fig. 7.—High-power photomicrograph of same tumor as Fig. 6, showing rare tubules among the interstitial cell masses.



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11 EAST CHASE STREET

pearance of this tumor was quite different from that of the first case, as it consisted almost entirely of interstitial cell elements with very occasional tubule formation. The predominance of interstitial cells in the tumor correlates well with the clinical findings of virulism and elevated 17-ketosteroids. This patient had a simple salpingo-oophorectomy and when last seen ten months postoperatively, she was menstruating regularly and the enlargement of the clitoris had regressed. However, there had been no improvement in the hirsutism or voice pitch, and she had not become pregnant.

These two cases again serve to emphasize the great variability in the development of symptoms as well as the microscopic picture in cases of arrhenoblastoma of the ovary. The amount and development of the interstitial cell tissue found in the tumor correlate well with the degree and rapidity of development of the masculinization of the patient.

As the arrhenoblastoma is a biologically active tumor, it would seem that certain hormone determinations might be of academic interest. Seventeen-ketosteroid determinations with fractionation of the alpha and beta substances would be especially helpful clinically in differentiating virulization due to adrenal hyperplasia or tumor and that due to an arrhenoblastoma. There are no such assays reported in the literature. One case has been reported in which a bio-assay for androgenic substances was performed.<sup>1</sup> This patient was excreting 51 eapon units of androgenic substances per 24 hours preoperatively. Postoperatively, the excretion fell to between 5 and 15 eapon units per 24 hours. Although 51 eapon units seem high for a normal female, the authors consider it to be within normal limits as the male excretion reaches 77 eapon units per 24 hours. Seventeen-ketosteroid determinations have been reported as normal on one case of an arrhenoblastoma of the Pick type.<sup>2</sup> The same authors state that they also found a normal 17-ketosteroid excretion in another case of arrhenoblastoma, but the pathologic type is not mentioned. In our one case on which such determinations were made, the 17-ketosteroid excretion was definitely elevated preoperatively.

The question of the malignancy of the arrhenoblastoma is difficult, as there have been only about 65 cases reported to date,<sup>3-20</sup> and the follow-up studies on these are not too satisfactory. However, as far as can be judged from the literature, the majority of cases are benign. In view of this, a simple oophorectomy seems advisable, especially as a great many of the tumors appear in young women in whom it is desirable to preserve the childbearing function.

It is an interesting pathologic observation that the arrhenoblastoma, like the dysgerminoma, shows a predilection for the right ovary. This is in keeping with the theory of its origin from the embryonic cell rests, as the right ovary develops more slowly and less completely both embryologically and phylogenetically, the right ovary in birds being almost entirely absent.<sup>21</sup>

### Summary

Two cases of arrhenoblastoma of the ovary have been reported. Both occurred in relatively young women and in the right ovary. One was associated with rather marked virulism, and microscopically was of the intermediate cell type. The other tumor, which was associated with only slight masculinization, was microscopically highly differentiated and resembled a tubular adenoma of Pick. The 17-ketosteroid excretion was studied in one case and proved to be elevated preoperatively, falling to normal within twelve days postoperatively. No pregnanediol was present in the urine in this case. A simple salpingo-oophorectomy was performed in one case, and the patient is well one year postoperatively with some regression of masculinization and regular menses. The other patient had a bilateral salpingo-oophorectomy and hysterectomy, and is well six months postoperatively.

TABLE I

AGE	DISTRIBUTION	
21-25	1	
26-30	3	
31-35	23	
36-40	110	A. 14 operators performed the 500 operations
41-45	127	B. 74.4 per cent of the cases are in the age group 36 to 50 years
46-50	135	C. There were 12 nulliparas and 1 virgin
51-55	46	
56-60	25	
61-65	18	
66-70	9	
71-75	2	
76-80	1	
	500	

TABLE II. PREVIOUS OPERATIONS

I. Previous plastics	14
II. Previous laparotomies	65
A. Appendectomies	28
B. Cholecystectomies	14
C. Cholecystectomy and appendectomy	12
D. Pelvic operations	11
Ectopic pregnancy	5
Ovarian cyst	4
Uterine suspension	1
Salpingectomy	1

TABLE III. GROUPING OF CASES

Fibroids	227	A. 17 of the cases were post-menopausal
Bleeding	252	B. 6 of the fundal carcinomas were diagnosed preoperatively
Prolapse	162	C. Both sarcomas were recognized as malignancies preoperatively
Hypertrophy or laceration of cervix	92	
Cystocele	226	
Carcinoma	7	
Sarcoma	2	
Sterilization	3	

Based on the preoperative clinical findings and the report of the pathologist, the cases could be grouped under the following headings:

1. Fibroids
2. Bleeding
3. Prolapse
4. Cystocele and/or rectocele
5. Hypertrophy and laceration of the cervix
6. Carcinoma
7. Sarcoma
8. Sterilization

Invariably there was a combination of two or more of these conditions which invited the decision to perform the vaginal operation. In 18 instances fibroids were the only clinical and pathologic findings. Fibroids and anomalous bleeding were the indications in 46 cases. Hypertrophy and laceration of the cervix, or cervicitis, alone were never a sole indication for the operation. The combination of prolapse and cystocele was the only indication in 31 cases. There were seven carcinomas of the fundus and two sarcomas of the fundus. Four of the carcinomas of the fundus had had previous radium treatment. In all these cases the patients were elderly or obese, and for that reason the vaginal procedure was selected; and, as noted above, hysterectomy was

## A STUDY OF 500 VAGINAL HYSTERECTOMIES

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**R**EPORTS emanating from various gynecologic clinics have proved that vaginal hysterectomy is an operation with a very low morbidity and mortality. In many large series ranging from 600 to 2,000 cases, the percentage of mortalities has varied from 0.0 per cent to 3.2 per cent; but the majority have been a fraction of 1 per cent. The other striking features in the reports of this operation are the rarity of shock or hemorrhage, the absence of trauma to the pelvic viscera, the minimum danger of infection, the applicability of the operation to the obese and the aged, the relatively smooth post-operative course, and the absence of hernia. The incidence of thrombophlebitis and pulmonary embolus is very low, and pulmonary complications are also much less common.

The patient over 40 years of age who presents herself with a history of anomalous bleeding and who, in addition, is found to have disease of the cervix, fibroids, polyps, cystocele, and/or rectocele is an ideal subject for vaginal hysterectomy. Usually, those with cystocele have varying degrees of descent of the uterus. The gynecologist is thus enabled at one sitting to remove a diseased cervix and fundus, and at the same time perform a repair of the anterior and posterior vaginal walls. Likewise, some method of urethral plication may be included in instances of associated urinary incontinence.

This paper is devoted to the study of 500 consecutive vaginal hysterectomies, with and without anterior and posterior vaginal wall repairs, performed on the gynecologic service at Beth Israel Hospital over a five-year period, from January, 1940, through 1944. A group of 14 operators took part in this work, all following a standardized fixation-ligature technique. A number of these cases were performed by three resident gynecologists who succeeded one another. The 500 cases include operations performed on private and clinic patients. It is of interest that over the same period of time an almost equal number of abdominal hysterectomies, supracervical and total, were performed.

### Results

The patients varied in age from 24 to 78 years; 74.4 per cent were in the age group 36 to 50 years; 88.6 per cent of the cases were performed by a group of eight of the 14 operators. There were 12 nulliparas in the entire group; and one of these women was a virgin (Table I).

Sixty-five, or 11 per cent of the cases had had previous laparotomies; and of this group 11 were in the pelvic surgery group, including tubal gestations, oophorectomies, one salpingectomy, and one uterine suspension. There were 14 instances in which a previous vaginal plastic procedure had been performed. The details of the previous vaginal procedures were usually not known, for in practically all the cases they had been performed at another hospital (Table II).

and both had anterior wall repair in common. The morbidity in the entire group was 24.5 per cent. Oophorectomy did not have any influence on postoperative morbidity. There were 8 pelvic infections in the entire series. Three of these were pelvic abscesses. Five were bilateral parametritides (three of these were associated with cervicitis). It is of interest to note that there is a definite rise in the percentage of morbidity as soon as the anterior wall is operated upon (Table VI).

One of the disturbing postoperative complications following vaginal surgery is urinary retention. This may be due in part to compression of the urethra and vesical neck from sutures and postoperative edema, interference with the contraction mechanism because of trauma to the bladder musculature and/or nerve injury, altered position of the bladder, anesthesia, the recumbent position, and probably some psychogenic factors. One or all of these may be contributory to the cause of the retention which, in turn, greatly increases the liability to cystitis, and thus the incidence of postoperative morbidity.

TABLE VI

OPERATION	NUM- BER	TEMPERATURE MORBIDITY		PELVIC POSTOP- ERATIVE INFEC- TION	WITH OOPHO- RECTOMY
		NUM- BER	PER CENT		
Vaginal hysterectomy	144	28	19.4	2	16
Vaginal hysterectomy and posterior colporrhaphy	103	16	15.5	1	12
Vaginal hysterectomy and anterior and posterior colporrhaphy	242	60		3	17
Vaginal hysterectomy and anterior colporrhaphy	11	2	24.5	2	2

The problem of bladder difficulties was investigated first by simply ascertaining how long it took the patient to begin voiding spontaneously. In the simple vaginal hysterectomy group it was 1.3 days on the average; 1.8 days in the vaginal hysterectomy and posterior colporrhaphy group; 4.8 days in the vaginal hysterectomy, anterior and posterior colporrhaphy group; and 8 days in the vaginal hysterectomy and anterior colporrhaphy group (Table VII). Invariably, once the patient had begun to void, she voided in gradually larger and larger amounts. These patients were catheterized once daily—postmicturial—for residual urine. It was a strict rule not to discharge a patient until the residual urine was less than 30 c.c. There was, of course, wide variation in all these cases, in the number of days it took before the patients began to void spontaneously.

TABLE VII

OPERATION	NUMBER	PUS IN URINE		DIFFICULTY IN VOIDING
		NUMBER	PER CENT	
Vaginal hysterectomy	144	10	6.9	1.3 days
Vaginal hysterectomy and posterior colporrhaphy	103	15	14.5	1.8 days
Vaginal hysterectomy, anterior and posterior colporrhaphy	242	42		4.8 days
Vaginal hysterectomy and anterior colporrhaphy	11	6	18.9	8.0 days

It was difficult to find strict criteria for making the diagnosis of cystitis. The picture was not constant. Urgency, frequency, and dysuria were too variable. The findings of pus cells in the urine (15 to 20 cells per high power field, with or without clumps) was therefore taken as evidence of cystitis.

performed as a sterilizing procedure in three cases. These patients were multiparas who, because of their medical complications, were not good operative risks for laparotomy.

There were 68 patients who had associated medical complications. Essential hypertension was most common and occurred in 52 cases. There were ten cases of diabetes, one of ulcerative colitis, one rheumatic heart disease, one diaphragmatic hernia, one of coronary artery disease, one peptic ulcer, and one of bilateral polycystic kidney disease (Table IV).

TABLE IV. ASSOCIATED DISEASES IN THESE PATIENTS

Essential hypertension	52
Diabetes	10
Ulcerative colitis	1
Rheumatic heart disease	1
Diaphragmatic hernia	1
Coronary artery disease	1
Peptic ulcer	1
Polycystic kidney disease	1

There were four types of vaginal operations performed in this series:

(a) Vaginal hysterectomy alone	144
(b) Vaginal hysterectomy and anterior colporrhaphy	11
(c) Vaginal hysterectomy and posterior colporrhaphy	103
(d) Vaginal hysterectomy and anterior and posterior colporrhaphy	242

When making studies of postoperative morbidity, surgeons have for many years been using the obstetric standard of morbidity, i.e., a rise in temperature to 100.4° F. on any two days after the day of operation. Obviously, because the work of the surgeon is so varied, it seemed unfair to accept this obstetric standard. In the present series only those cases were considered morbid where there was a rise in temperature to 100.4° F. after the fourth postoperative day. Using this standard of morbidity, it was found that 106, or 21.2 per cent, of the 500 cases were morbid.

Many of these patients were given sulfonamides as prophylaxis against urinary tract infections. Of 193 cases receiving sulfonamides, 46, or 23 per cent, were morbid. Three hundred and seven did not receive sulfonamides and, of these, 56, or 18 per cent, were morbid. One hundred and sixteen of the cases were reported by the pathologist to have had gross and microscopic cervicitis. In this group, 25, or 21 per cent, were morbid. Of the 384 cases without cervicitis, 77, or 20 per cent, also showed morbidity (Table V). One notes that there was very little influence upon the morbidity rate, despite the use of sulfonamides or the presence of cervicitis.

TABLE V. MORBIDITY

	NUMBER	NUMBER MORBID	PER CENT
All cases inclusive	500	106	21.2
Cases which received sulfonamides prophylactically	193	46	23.0
Cases not receiving sulfonamides	307	56	18.0
Cases with pathological report of Cervicitis	116	25	21.0
Cases without cervicitis	384	77	20.0

In the group where vaginal hysterectomy alone was done (144 cases), the morbidity was 19.4 per cent; vaginal hysterectomy and posterior colporrhaphy (103 cases), 15.5 per cent. Vaginal hysterectomy with anterior and posterior wall repair and vaginal hysterectomy with only anterior wall repair were combined as one group (253 cases). The latter group consisted of only 11 cases

favorably with the group of uteri not surgically diminished in size before removal. Of the 58 uteri which were the size of a three-month gestation or over, 8, or 15.1 per cent, were followed by morbidity.

TABLE IX

A.	87 of the 500 uteri had some form of treatment in order to reduce their size, thus facilitating delivery into the vagina
B.	49 were subjected to only one of the above procedures
C.	38 were treated by a combination of these procedures
D.	23 of the 87, or 26.4 per cent, were followed by temperature morbidity
E.	58 uteri were the size of a 3 months' gestation or more; 8 of these cases, or 15.1 per cent, were morbid
	(1) 1 pelvic abscess with pelvic peritonitis
	(2) 1 case of phlebitis

As was mentioned before, there were seven carcinomas of the fundus and two sarcomas. In all of these cases the uterus was either normal in size or only slightly enlarged, and still freely movable. The diagnosis in all was known preoperatively, and four of the carcinoma cases had had previous radium. All of these patients were either obese or in the older age group, and thus not good operative risks for abdominal surgery (Table X).

TABLE X. MALIGNANCIES

I. Carcinoma of the fundus	7
(a) 6 are still alive after 1 to 4 years	
(b) 3 were postmenopausal bleeding cases	
II. Adenoacanthoma	1 no follow-up
III. Sarcoma	2
(a) Endometrial sarcoma (Frank)	1
Despite local vaginal metastases, this patient is alive and well after 5 years; local metastases were treated with radium	
(b) Myosarcoma	1 no follow-up

Vaginal hysterectomy is contraindicated in the following instances: pelvic inflammatory disease, endometriosis with fixation of tissues, intraligamentous tumors, the presence of a large ovarian cyst, malignancy with fixation, post-radiation fixation, ventral fixation of the uterus, or previous amputation of the cervix with shortening of the cardinal ligaments. Nulliparity is no contraindication, for here, once the cervix is circumcised and the pubocervical fascia cut, along with the cardinal ligaments, the uterus may be made accessible. A previous laparotomy is no contraindication, except when a gynecologic operation has been performed.

The one death in this series makes for a mortality rate of 0.2 per cent. After a somewhat morbid course terminating finally with about five days of temperature at 99° F., this patient was discharged from the hospital in apparently good condition. Soon after reaching home she had sexual intercourse. Two weeks later she presented herself again with signs and symptoms of pelvic abscess and pelvic peritonitis. She developed, despite colpotomy and intense chemotherapy, a perinephric abscess and died. There was one case of pelvic phlebitis and pulmonary infarct, three of pyelonephritis, one of transient pulmonary edema, one of transient auricular flutter, and three cases of pneumonia. Early in the series there were two instances of bladder injury. Both times the opening was promptly closed in layers. One of these patients developed a pyelonephritis. Otherwise these two cases ran the usual postoperative

Of the 500 cases, 73, or 14.6 per cent, developed pus in the urine—34 of these had received sulfonamides prophylactically.

In the group of 144 vaginal hysterectomies, 10 cases, or 6.9 per cent, developed cystitis—15 of the 103 cases of vaginal hysterectomy and posterior colporrhaphy, or 14.5 per cent, also showed pus in the urine. The large group of vaginal hysterectomy with anterior and posterior wall repair (242 cases) and the small group of vaginal hysterectomy and anterior wall repair (11 cases), were analyzed as one group. Here, 48 cases, or 18.9 per cent, developed cystitis. The evidence thus seems to point to the fact that when operation upon the anterior vaginal wall is performed, the incidence of cystitis increases (Table VII).

Simple catheterization was used in 429 of the cases. The remaining cases received either a retention catheter or tidal drainage. One hundred and ninety-three of the entire group of 500 had received sulfonamides prophylactically. There are as yet too few cases to analyze each of these groups and to evaluate the merits of each of the forms of postoperative bladder care. At the moment, however, it is an impression that careful, repeated catheterization, with administration of sulfonamides prophylactically, is the procedure of choice.

The presence of large fibroids in itself is not a contraindication to the procedure of vaginal hysterectomy. In the present series, some uteri were removed which were almost the size of a five months' gestation. Relaxation of the anterior and posterior vaginal walls, descent of the cervix, and mobility of the uterus are aids in making for the ease of vaginal extirpation of the uterus. To facilitate delivery of the uterus into the vagina, several methods can be used, namely: morcellation, amputation of the cervix, bisecting the fundus, and coring out the fundus of the uterus, as described by Lash. Caution is advocated in those instances where intraligamentous, subvesicle, and cervical fibroids are present, because these cases are associated with variations from the normal anatomic relationships of the ureters and bladder, and injuries to these organs may occur. These complications may thus contraindicate vaginal hysterectomy.

Only 85 of the entire 500 uteri removed were of normal size. Two hundred and eighty-four of them were the size of a six- to eight-week gestation, 73 the size of a ten- to eleven-week gestation, 34 the size of a three-month gestation, and 24 over the size of a three-month gestation. Thus, 58, or 11.6 per cent, were the size of a three-month gestation or over (Table VIII).

TABLE VIII

SIZE OF UTERUS				
NORMAL	6 TO 8 WEEKS	10 TO 11 WEEKS	3 MONTHS	OVER 3 MONTHS
85	284	73	34	24
				11.6%
METHOD OF TREATMENT TO FACILITATE DELIVERY OF UTERUS				
MORCELLATION	AMPUTATION OF CERVIX	CORING OUT OF UTERUS	BISECTION OF FUNDUS	
47	65	12	47	

Eighty-seven of the 500 uteri had some form of treatment in order to reduce their size. Forty-nine were subjected to only one of the above procedures. Thirty-eight were treated by a combination of them. Morcellation was carried out 47 times, amputation of the cervix 65 times, bisection of the fundus 47 times, coring the fundus 12 times (Table IX). Twenty-three of the 87, or 26.4 per cent, were followed by temperature morbidity, the average morbidity lasting four days. Hence the morbidity in this group compares



the size of the uterus. Uteri up to the size of a three-month gestation have been removed with relative facility. Uteri the size of a four- to five-month gestation have been removed.

7. Cystitis is the commonest cause of morbidity postoperatively in vaginal hysterectomy. Difficulty in voiding disappears in the majority of cases within several days.

8. The development of ovarian cysts after vaginal hysterectomy is an uncommon complication.

9. The fixation-ligature technique is safe, and readily taught and learned.

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ONE WEST EIGHTY-SIXTH STREET

course of the vaginal hysterectomy. There were no urethral injuries, injuries to the rectum, or vesicovaginal fistulae. Twice there was postoperative bleeding from the vaginal cuff, and twice from the perineum. Two of the cases have returned with symptomatic ovarian cysts which were removed. One was a simple serous cyst and the other a chocolate cyst. It is noteworthy at this point to mention the infrequency of development of ovarian cysts after vaginal hysterectomy (Table XI).

TABLE XI. COMPLICATIONS

Deaths		1
(Morbid course. Discharged 15th day. Returned 2 weeks later with pelvic abscess, pelvic peritonitis, and a perinephric abscess. Colpotomy)		
Injury to bladder		2
(Occurred early in the series. Promptly recognized and repaired. No vesicovaginal fistula)		
Vaginal abscess		1
Bleeding postoperatively		4
(a) Vaginal cuff	2	
(b) Perineum	2	
Ovarian cyst		2
(Developed after vaginal hysterectomy. These were confirmed at subsequent operation)		
(a) Serous cyst	1	
(b) Chocolate cyst	1	
Pyelonephritis		3
Pulmonary infections		3
(a) Tracheobronchitis	1	
(b) Virus pneumonia	1	
(c) Bronchopneumonia	1	
Transient pulmonary edema		1
Transient auricular flutter		1

No originality is claimed in the gross aspects of the technique of vaginal hysterectomy as performed at Beth Israel Hospital. However, the technique is a rational, methodical, and safe one; and it is easily taught. It has a definite place in the gynecologist's armamentarium and, once the technique is mastered, and as skill and experience increases, the surgeon will find himself using it more frequently.

### Conclusions

1. Vaginal hysterectomy is an operation associated with a minimum of shock and hemorrhage, low morbidity, and low mortality.
2. Where hysterectomy is indicated, the vaginal approach is the procedure of choice in the obese and the aged.
3. Nulliparity is no contraindication to vaginal hysterectomy.
4. Where there are pathologic changes in the uterus and there is associated cystocele and/or rectocele, vaginal extirpation of the uterus along with plastic repair of the vagina is wisest.
5. Cervicitis, sulfonamides, oophorectomy, and age have relatively little effect on morbidity.
6. Morcellation, amputation of the cervix, bisection of the fundus, and coring out of the fundus of the uterus have been the procedures for reducing

TABLE I. THE INCIDENCE OF THE ETIOLOGIC FACTORS IN 257 COUPLES WITH PRIMARY OR SECONDARY STERILITY

FACTOR	NO. OF CASES	PER CENT
I. Cervical factor	97	38
a. Inadequate invasion of cervix	66	68
b. Failure to deposit sperm	31	32
II. Tubal damage	140	54
a. Partial occlusion	90	64.3
b. Total occlusion	50	35.7
III. Endocrine factors in female	134	52
a. Amenorrhea	49	36.5
b. Metrorrhagia	3	2.3
c. Anovular menstruation	82	61.2
IV. Male infertility or absolute sterility	106	41
a. Endocrine azospermia	5	4.7
b. Obstructive azospermia	15	14.2
c. Endocrine oligozoospermia	5	4.7
d. Obstructive oligozoospermia	71	66.9
e. Necrozoospermia	10	9.5

In 205, or 79%, a combination of two or more of the four major factors coexisted.

of these became pregnant. Pelvic lesions were eliminated, when possible, before sterility studies were begun. The patients with chronic salpingitis were not studied from the standpoint of sterility.

Tubal damage was the most frequently encountered sole or associated cause of sterility. Of the 257 patients, 90 had partial and 50 had total occlusion of the Fallopian tubes, as one of two or more etiologic factors in barren marriage, for a total of 54 per cent. In 61 cases, or 23.7 per cent, tubal occlusion was the sole cause of the sterility. All patients received pelvic diathermy and estrogenic therapy for one month, and once monthly transuterine insufflations. Of 53 patients receiving repeated transuterine insufflations as one therapeutic measure, 43, or 81 per cent, conceived. Four patients conceived after one Rubin test. These were considered incidental pregnancies. Iodized oil instillations—lipiodol—were resorted to when other modes of therapy failed. Of 35 patients so treated, 12, or 34.2 per cent, conceived. One pregnancy followed removal of one tube with a plastic on the other. Of 140 patients treated for tubal occlusion, 66, or 47 per cent, conceived. Twenty-two of 50 patients with total occlusion conceived, i.e., 44 per cent, and 44 of 90 patients with partial occlusion conceived, i.e., 48 per cent.

Failure of deposition of spermatozoa by fertile mates or inadequate invasion of the cervical canal, the cervical factor in sterility, was one of two or more factors in the barrenness of 97, or 38 per cent, of the cases. The failure to deposit spermatozoa in the vicinity of the external cervical os, as determined by the Hühner test, was in most instances found to be due to faulty technique at intercourse. Premature ejaculation, redundant vaginal walls, and vaginismus were less frequently the cause for failure of deposition of the spermatozoa in the vagina. Total absence or inadequate invasion of the cervical canal, despite the presence of the usual number of spermatozoa in the posterior fornix following several hours after intercourse, was present in 66, or 69 per cent, of the cases where the cervical factor was a cause of barrenness. The most common cause of the absence of spermatozoa in the cervical canal, when an adequate number of them was present in the posterior vaginal fornix, was a pinhole external os with viscid mucus therein and intracervical polyps. The most common cause of inadequate invasion of the cervical canal was oligozoospermia and lack of vitality of the spermatozoa as determined by a properly performed semen examination.

## AN ANALYSIS OF 257 CASES OF STERILITY\*

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THIS presentation is based on a study of 257 barren marriages, treated in the outpatient department of Mount Sinai Hospital and in the private office of Dr. Charles Mazer, during the five-year period, 1940 to 1944, inclusive.

The problem of sterility is one that confronts every obstetrician and gynecologist. Multiple etiologic factors enter into the genesis of the majority of sterile marriages. It is only through a systematic study of the sterile couple that a solution may be reached. All factors, no matter how insignificant, should be investigated. Perseverance on the part of the physician and the patient is essential. The road to success is long and has many obstacles.

### Method

The following mode of study was employed. General studies included a complete physical examination, and laboratory studies, consisting of a complete blood count, urinalysis, blood Wassermann and chemistry, and cervical smears. Special studies, included the following: (1) A Hühner test, to determine whether semen is deposited, whether there is adequate invasion of the cervical canal, and whether there is any hostility of the cervical secretions. (2) A Rubin test or/and hysterosalpingography, to determine the degree of patency of the Fallopian tubes, site of obstruction, and the presence of intrauterine pathology. (3) Endocrine studies, relating to abnormalities of the menstrual cycle and anovular menstruation. These studies included endometrial biopsy, vaginal smears, estrogen determinations, and the basal body temperature.

### Results

Of the 257 cases of barren marriages, 53, or 20.6 per cent, were of secondary sterility and 204, or 79.4 per cent, of primary sterility. The duration of the sterility ranged from one to twenty years, with an average of five years. The age incidence was from 20 to 39 years, with an average of 28.2 years. In 205 of the 257 cases, or 79 per cent, a combination of two or more etiologic factors co-existed.

After the patient was thoroughly investigated as to the causative factors involved, these were evaluated and therapy instituted. Adequate treatment consisted in following persistent efforts to eliminate the impediments to conception for at least one year. It was difficult to limit the span of time for adequate treatment, as patients differ, but failure within one year of continuous treatment portended a poor prognosis.

In the evaluation of the therapeutic agent employed, credit was given to the one that eliminated the major cause of the sterility. Other measures were labeled therapeutic adjuncts. Best results were obtained in the presence of a single etiologic factor. These patients, after conceiving, were treated with care usually given habitual aborters.

Seventeen, or 6.6 per cent, of the patients had gross pelvic pathology, such as large fibromyomas, ovarian cysts, and chronic salpingitis. Myomectomies were performed on four patients, three of whom conceived and carried to term. Three ovarian cysts were resected leaving portions of the ovary involved. One

\*Read before the Philadelphia Obstetrical Society, March 7, 1946.

Of 82 cases treated for anovular menstruation 41, or 50 per cent, conceived. Thirty-four patients received equine gonadotropin; 15, or 44 per cent, of these conceived, one of these aborted. Of 19 patients treated with Synapoidin, 12, or 63 per cent, conceived, and one of these aborted. Of 29 patients receiving pregnant mare serum plus chorionic gonadotropin, 14, or 48.2 per cent, conceived.

In 106, or 41 per cent of the cases, the husband was partly or wholly at fault for the sterility. Of these, 68, or 64.1 per cent, conceived following therapy of the husband simultaneously with treatment of his mate for conditions unrelated to the low degree of fertility of the husband. Absolute sterility in the male was rare, it was found in only ten cases, i.e., 9.4 per cent. Eighty-six cases, or 81.1 per cent, had oligozoospermia and varying degrees of necrozoospermia. In ten, or 9.4 per cent, of the cases an endocrine dysfunction was found in the male. An urologist treated all males.

Of the 257 cases studied, 129, or 50 per cent, conceived following therapy. There were seven abortions and one ectopic. There were no stillbirths or neonatal deaths.

TABLE III. RESULTS IN PRIMARY AND SECONDARY STERILITY

NUMBER OF PATIENTS	PRIMARY STERILITY	SECONDARY STERILITY	AGE INCIDENCE	AVERAGE DURATION OF STERILITY	NUMBER OF PREGNANCIES	PER CENT OF PREGNANCIES
257	204	53	28.2 yr.	5 yr.	129	50

TABLE IV. TERMINATION OF THE 129 PREGNANCIES

	NUMBER	PER CENT
Living infants	122	93.8
Spontaneous abortions	7	5.4
Ectopic pregnancies	1	0.8
Stillbirths	0	
Neonatal deaths	0	

### Summary

In conclusion, several interesting features may be pointed out. One patient conceived and delivered after one ectopic pregnancy. One pregnancy followed the removal of one tube with a plastic on the other. One homologous insemination was attempted with success. One pregnancy resulted from four heterologous inseminations. Of prime interest was the use of lipiodol as a therapeutic agent for occluded tubes. Out of 35 patients so treated, 12 conceived. Of 32 patients treated for amenorrhea with x-ray to the pituitary and ovary, 28 conceived. Thirty-four patients were treated with pregnant mares serum for anovular menstruation. Fifteen of these conceived. Synapoidin was used in 19 cases, 12 pregnancies followed.

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Of the 97 patients in whom either failure of deposition of the semen or lack of invasion of the cervical canal was a contributing cause 73, or 75 per cent, conceived, following treatment of the several factors involved. The treatment of inadequate invasion of the cervical canal consisted of the removal of obstructive agents, such as pinhole os, cervical polyps, and viscid cervical secretions. Twenty-six patients, or 39 per cent, conceived following this form of therapy. Preeoital alkaline vaginal douches or Nutrisal were employed in instances of oligozoospermia and partial neerozoospermia in the hope of maintaining the vitality of the spermatozoa deposited in the posterior vaginal fornix. Homologous insemination of the cervix was employed when all other measures failed. It was successful in the single case employed.

Of 134 patients that showed endocrine menstrual disturbances, alone or in combination with other causes, 54, or 42 per cent, conceived following therapy, toward elimination of this and other causes of the barren marriage. The following menstrual disturbances were found: amenorrhea, menometrorrhagia, and anovular menstruation.

Of 49 patients treated for amenorrhea 29, or 59.1 per cent, conceived. Low dosage irradiation to the pituitary and ovary was the most effective form of therapy. Of 32 cases so treated, 28, or 87.5 per cent, conceived. Therapeutic adjunct included small doses of thyroid, regardless of the basal metabolism rate, correction of faulty diet, insulin for the underweight, and removal of foci of infection.

Of three patients treated for menometrorrhagia, one conceived following dilatation and curettage followed by chorionic gonadotropin.

TABLE II. ANALYSIS OF ADEQUATE TREATMENT IN 257 COUPLES WITH PRIMARY AND SECONDARY STERILITY

PRESUMED ETIOLOGIC FACTOR	NO. OF PATIENTS TREATED	MOST IMPORTANT THERAPEUTIC AGENTS USED	THERAPEUTIC ADJUNCTS	NO. OF PREGNANCIES
I. <i>Cervical Factor</i>	97			73
a. Inadequate invasion of cervix		Dilatation and cauterization of cervix. Homologous insemination	Preeoital alkaline douche. Treatment of male	
b. Failure to deposit sperm		Vaginismus operation	Treatment of male	
II. <i>Tubal Factor</i>	140			66
		Repeated transuterine insufflation	Diathermy, estrogen thyroid. Cauterization of cervix. Treatment of male	
		Lipiodol instillations in uterus		
III. <i>Endocrine Factor</i>	134			54
a. Amenorrhea	49	Low dosage irradiation	Desiccated thyroid—all. Treatment of male. Equine gonadotropin	29
b. Metrorrhagia	3	Curettage. Chorionic gonadotropin	Desiccated thyroid	1
c. Anovular menstruation	82	Equine gonadotropin. Synapoidin. Equine and chorionic gonadotropin	Desiccated thyroid	41
IV. <i>Male Infertility</i>	106			68
a. Azospermia	20	Combinations of pituitary, equine, and chorionic gonadotropin	Thyroid and massage of prostate	
b. Oligozoospermia	86	Pituitary and equine gonadotropin	Thyroid and pre-coital alkaline douches	

## SADDLE BLOCK ANESTHESIA WITH NUPERCAINE IN OBSTETRICS

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THE term, saddle block, is applied to a form of low spinal anesthesia confined exclusively to the perineal area. The technique for its induction has been described by both British and American writers. Pitkin, in 1928,<sup>1</sup> appears to be the first American writer who described a technique for producing this distribution of anesthesia. The block is ideal for perineal and rectal surgery. However, it failed to gain widespread popularity because the anesthesia did not remain localized in the originally intended spinal segments but spread over a more extensive area. This difficulty has been overcome by adding glucose to the solution of the drug.<sup>2</sup> Apparently, the glucose inhibits diffusion and, in addition, causes the solution to be hyperbaric or heavier than spinal fluid. When injected into the subarachnoid space with the patient in the sitting position, the solution gravitates downward and the drug becomes concentrated in the cone of the dural sac. Exact localization of anesthesia is thus possible. One desirable feature of the block, particularly from the standpoint of obstetrics, is that the distribution of anesthesia may be modified by varying the time the patient remains in the sitting position after injection. Thus, one can, by certain manipulations, obtain complete loss of sensation in the perineum and relaxation of the perineal muscles and hypalgesia and analgesia over the legs and thighs without paralysis of the thigh and leg muscles. This distribution of anesthesia is desirable when the lithotomy position is indicated. In addition, the sensory fibers to the uterus are affected and the pain of labor is abolished. This distribution of anesthesia and analgesia resembles, in many ways, that distribution obtained by peridural (caudal) injection of local anesthetic drugs. Inasmuch as saddle block is merely a specialized form of a subarachnoid block, its induction is simpler, safer, and more precise than that of a caudal block.

Heretofore, spinal anesthesia has been of limited value in obstetrics. One reason for the lack of enthusiasm has been that procaine has been the drug of choice. It is necessary to repeat the block frequently for analgesia early in labor when procaine and drugs of similar duration of action are used. The longer-acting and more potent drugs, such as pontocaine and nupercaine, have extended the usefulness of spinal anesthesia by the single injection method. Nupercaine, which possesses a duration of action ranging from three to five hours, has been used by certain workers for general surgery. Cosgrove<sup>3</sup> used it for obstetric anesthesia in 1930 but obtained unsatisfactory results. The extent of anesthesia was difficult to control, and he noted a high incidence of nausea, vomiting, and postlumbar puncture headaches. His experience, however, is not in accord with that of other workers using nupercaine. Jones,<sup>4</sup> Whitacre, and

## Discussion

DR. ARTHUR FIRST.—This is a statistical paper and it is difficult to discuss a statistical paper without quoting more statistics. One becomes confused by the many figures and percentages and in the resultant haze may miss the essence which is that thorough treatment of many factors in sterility plus persistence in treatment over one year, plus careful anti-abortion therapy after a patient finally conceives, yields the best results.

Dr. Winson finds that 20 per cent of his sterile patients had been pregnant previously. It is with the remaining 80 per cent that the most difficult problems are encountered. He divides his cases into four etiologic factors, namely, the male factor, the cervical factor, the tubal factor, and the endocrine factor.

As to the male factor, the husband was responsible in 40 per cent, which is the usual figure quoted. It would be interesting to know how many of those became pregnant following treatment to the male only. My own experience has been rather disappointing from the standpoint of improvement in sperm count and of male fertility in spite of thyroid, vitamin E, amino acids, and hormone injections. Massage of the prostate and seminal vesicles, thus getting rid of pus in the prostatic secretion, seems to be our most effective agent at present.

As to the cervical factor, Dr. Winson mentions precoital alkaline vaginal douches or so-called nutrisal. In our experience the addition of this Ringer's glucose solution has meant little. Dr. Winson mentions one case of homologous insemination resulting in pregnancy. We have used this form of treatment for over ten years where there is a question of faulty insemination. I put the entire semen from the husband in a diaphragm and this is placed against the cervix for twenty-four hours on three different occasions during the fertile period. Our results are encouraging.

As to the tubal factor, the 24 per cent tubal occlusion noted as the sole cause of sterility runs much lower than that obtained in a hospital sterility clinic. At our sterility clinic at Jefferson Medical College, over 60 per cent of the patients have completely blocked tubes. Of interest is the value of lipiodal injection as a therapeutic measure. Twelve out of 35 patients becoming pregnant is certainly an excellent percentage. From personal experience, however, I would recommend that this procedure be employed only in the hospital; as on several occasions where I have allowed the patient to go home immediately, she suffered a violent attack of pain a few hours subsequently which was relieved only with morphine.

As to the endocrine factor, the best results obtained by Dr. Mazer were with low dosage irradiation of the pituitary gland for amenorrhea and employing practically all the gonadotropic and ovarian hormones in the pharmacopeia for the other forms of endocrine sterility. Dr. Mazer employs very large and expensive dosages of these hormones which I think accounts for his unusually high degree of success, namely, 54 per cent.

In conclusion, I would like to say that Dr. Mazer and Dr. Winson are to be congratulated on their excellent average of 129 pregnancies out of 257 sterile women. However, I think more practical information could be obtained from this paper if typical case histories were summarized in table form with dosages, etc., rather than giving us an over-all picture of figures and percentages.



The sensory and autonomic fibers of a mixed nerve are more sensitive to the effects of a local anesthetic drug than the motor. When the patient is promptly restored to the recumbent position, a  $2\frac{1}{2}$  mg. dose becomes distributed over a greater number of segments than if she sits up thirty seconds. The lumbar segments, however, are exposed to a more dilute solution than the sacral. The degree of anesthesia decreases as one ascends the cord. Still, the concentration of drug is sufficient to produce anesthesia and paralysis of the legs, thighs, and hypogastric areas in most cases. The sacral segments are exposed to a more concentrated solution of drug than the lumbar so that both motor and sensory fibers are profoundly affected. The perineal area, therefore, is completely relaxed. When the patient sits up thirty seconds, a greater concentration of drug localizes in the conus than in the former case. Anesthesia of the vulva and other perineal structures, likewise, is complete. The concentration of drug along the lumbar segments is less and, as a rule, insufficient to block completely all the sensory fibers in these segments. Hypalgesia and disseminated areas of analgesia are present in the legs and thighs. Little or no paresis of the leg and thigh muscle is obtained. The analgesia over the thighs gradually merges into an area of hypalgesia over the lower abdomen, sometimes as far as the umbilicus. However, the concentration of the drug is sufficient to block the sensory fibers to the cervix and uterus. The sensory fibers to the cervix and lower uterine segments are derived from the sacral and lower lumbar spinal nerves, those of the upper part and the fundus from the upper lumbar and twelfth thoracic segments. The motor innervation of the uterus is still a matter of question. It is believed that the motor fibers are derived from the lower thoracic segments. Consequently, there is no diminution in the number or force of the contractions unless the drug extends into the thoracic region. The recti are not affected and the patient can bear down if requested. The patient will not bear down unless told to do so, however, as the analgesia causes her to be unaware of the contractions.

### Method of Study

The writers have been interested primarily in the applicability of the block to obstetrics. Therefore, in order to exclude all complicating factors, its use was limited exclusively to normal primiparas or multiparas. Patients presenting systemic abnormalities or obstetric complications were excluded. Sedation, likewise, was omitted in the first 100 patients. The block was performed after the inception of the first stage of labor. Usually, the contractions appeared at 3- to 4-minute intervals and the cervix was 5 to 6 cm. dilated and approximately 60 to 80 per cent effaced. Blood pressure and pulse rate were observed at 3- to 4-minute intervals, shortly after induction of analgesia, and at 10- to 15-minute intervals after the first thirty minutes. The anesthetist remained in constant attendance in all cases, closely observing the frequency and intensity of contractions, fetal heart tones, progress of labor, respiration, and other reactions of the patient. Emphasis cannot be placed too strongly upon the fact, in this procedure as in other forms of subarachnoid anesthesia, that the patient may not be left unattended until ready for delivery. In approximately half the cases, analgesia was induced in the patient's bed. In the remaining cases, the block was induced in the delivery room, and the patients remained on the delivery table throughout labor. An anesthesia machine was in readiness for the administration of oxygen or artificial respiration or analgesia in the event that the block failed. Vasopressor drugs for overcoming hypotension were held in readiness as is the usual custom in all cases of spinal anesthesia. A second tray with drugs and needles was available for repeating the block for cases in which labor outlasted analgesia. In instances in which the block was repeated, the procedure was exactly as in the first block.

Sankey,<sup>5</sup> Silvertown,<sup>6</sup> Wilson,<sup>7</sup> and many other American and British workers have employed the drug with a high degree of satisfaction in all types of surgical procedures. Roman and Adriani<sup>8</sup> simplified the technique for using nupercaine for general surgery by mixing it with glucose and now use the drug for all lengthy operations at the Charity Hospital at New Orleans. Likewise, they have obtained a high degree of satisfaction with saddle block for rectal, urologic, and gynecologic surgery in which nupercaine was the drug of choice. There appeared to be no reason why saddle block using nupercaine could not be applied to obstetrics.

This is a report of a detailed study of its use for analgesia during labor and anesthesia for delivery in 136 obstetric patients.

### Technique

The materials for performing a saddle block are those usually employed in spinal anesthesia—a wheel needle, a 20 gauge short bevel spinal needle, and several 2 c.c. syringes. Glucose, 10 per cent, prepared in physiologic saline or distilled water, a 1/200 solution of nupercaine, and 1 per cent procaine for infiltration are the necessary solutions and drugs.

Two and one-half mg. of nupercaine ( $\frac{1}{2}$  c.c. of 1/200 solution) is thoroughly mixed with  $\frac{1}{2}$  c.c. of glucose solution and set aside in a 2 c.c. syringe. No spinal fluid is necessary in the preparation of the solution. It is preferable to prepare the solution before the lumbar puncture is performed to avert failures due to dislodgement of the needle by unexpected movements of the patient. The puncture must be performed with the patient in the sitting position. The puncture is simplified if the patient sits in the center of the delivery table or at the edge of the bed with the arms folded across the chest. She should lean forward with her shoulders supported by an assistant. An intradermal wheal is raised at the fourth lumbar interspace and the interspinous tissues are infiltrated with 1 per cent procaine. The third interspace may be employed if the fourth is not accessible. The use of the higher interspace does not appear to cause any appreciable difference in the extent of anesthesia. When spinal fluid flows freely the syringe containing the solution is attached to the needle and aspiration is attempted. A free flow of spinal fluid must be obtained to assure correct placement of the bevel of the needle in the subarachnoid space. In executing the maneuver, one should aspirate as little spinal fluid as possible (not more than  $\frac{1}{10}$  c.c.), otherwise dilution occurs which interferes when obtaining the desired distribution of anesthesia. The needle should be readjusted until a satisfactory flow is obtained if the spinal fluid does not flow freely. Most failures in spinal anesthesia are due to unsatisfactory lumbar puncture. The solution is injected as rapidly as gentle pressure upon the plunger of the syringe permits. The total time for completion of the injection is approximately two seconds. If the drug is injected slowly, the distribution of anesthesia will not be satisfactory. The needle is then withdrawn from the spinal canal and the patient is allowed to remain in the upright sitting position for thirty seconds, after which time she is placed in the recumbent position. This timing is particularly important and should be done by the clock. It is advisable to support the head on a pillow for at least fifteen minutes. The solution should not be introduced during a contraction because the spinal fluid pressure is increased at this time. Currents established in the subarachnoid space force the drug into the thoracic region and give greater distribution of anesthesia and halt labor. The patient must not move or shift about for five or ten minutes after completion of the injection. The straining, which may accompany such movements, also causes spreading of the drug in the spinal canal.

ephedrine (15 to 30 mg.) intravenously. The number of spinal segments affected in saddle block is few, and the motor anesthesia is confined to a few small muscles. Physiologic changes, therefore, are less extensive and profound than in "high" spinal anesthesia.

Respiratory depression or embarrassment was not encountered in any case. Rectal or urinary incontinence during labor was not observed. Hysterographic and other studies of the effects of the block upon labor were not attempted. No remarkable effect upon the duration of labor was apparent, however.

Postspinal headache, although not encountered in any case in this series, is the one complication which could limit the usefulness of the block. Backache, urinary retention, distention, ileus, meningismus, palsies, or other complications were, likewise, absent.

### Comment

Obviously, 136 cases is not a sufficient number to prove the merits or demerits of any method of analgesia or anesthesia. However, the number is sufficient to show the applicability of saddle block to obstetrics. Although the results were gratifying and untoward reactions were not encountered either during labor or delivery, one must bear in mind that the usual hazards and complications of spinal anesthesia may occur with this method as with others. The absence of headache, palsies, urinary retention, and other sequelae of spinal anesthesia in a series as small as this obviously is of no significance. Likewise, it must be emphasized that these were normal cases, free from complications. The applicability of this method of analgesia to other than uncomplicated obstetric cases requires further detailed study of a large series of cases. When spinal anesthesia is desired and not contraindicated, certainly, this is the technique of choice.

Saddle block anesthesia with nupercaine offers many advantages over the continuous caudal technique. The uncertainty of locating the caudal canal, the presence of the indwelling needles and catheters, the repeated use of relatively large amounts of local anesthetic drugs, and the uncertainty of distribution of anesthesia are undesirable features which are eliminated by saddle block.

### Summary

Saddle block anesthesia is a form of low spinal anesthesia distributed chiefly to the perineal area. A technique is described for producing prolonged anesthesia and analgesia by using nupercaine. The block was used in 136 normal cases with gratifying results. The ease and simplicity of induction, the safety allowed by the low dosage of drug, and the exact localization of the distribution of anesthesia make the use of this block the technique of choice where spinal anesthesia is preferred or desired in obstetrics. The method is worthy of further use and clinical trial.

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## Results

Satisfactory analgesia during labor and anesthesia at the time of delivery were obtained in the majority of cases. The average duration of analgesia was three hours. In some cases, the block lasted as long as five hours. In the majority of cases the pain of uterine contractions returned in three hours, but the perineum was still anesthetized. Eighty-one per cent of the patients obtained complete pain relief during labor and delivery. Fourteen per cent complained of slight pain in the upper abdomen upon application of forceps and a dragging sensation during the period of traction. In others, the traction caused a dull ache in the epigastrium or along the back in the lumbar region. No pain was felt in the perineum at this time or during repair of the episiotomy. Inhalation of analgesic mixtures of nitrous oxide-oxygen until the head was delivered obliterates this most satisfactorily. Surgical anesthesia with the gas with loss of consciousness is not necessary. In 5 per cent of the cases the block was not satisfactory. Pain in the perineum or back due to poor distribution of analgesia resulted. Pain from uterine contractions, likewise, was not relieved. The failure, it was felt, was due to some error in technique. It is imperative that timing and measurements of volume of solutions be precise to insure success. The block was repeated after fifteen minutes and satisfactory analgesia was obtained the second time in every case. There is no objection to, or danger in, repeating the block in the event of failure because the doses of nupercaine employed are small.

The patients were comfortable and cooperative throughout the labor and delivery. Patients in pain or who were not cooperative before the block was performed invariably became quiet and cooperative as soon as analgesia was established. The absence of paralysis of the extremities permitted the patient to move about in bed and shift to comfortable positions. The hypotension and other circulatory changes caused by postural changes when extensive anesthesia is obtained by subarachnoid block were not present in these patients. The analgesia in the legs and thighs averts the discomfort usually experienced when the lithotomy position is instituted during the delivery. Seventy per cent of the patients were delivered by aid of low forceps and episiotomy. Anesthesia for repair of episiotomy was satisfactorily obtained in every single instance. A single block was sufficient in 68 per cent of cases. In 32 per cent, labor outlasted analgesia and repeated blocks were necessary. The shortest time from the institution of analgesia until delivery was fifteen minutes; the longest was eleven hours and fifty-one minutes. In the latter case, three blocks were performed. No difference was noted in the third stage of labor if compared with cases delivered with other types of analgesia or anesthesia. Postpartum hemorrhage was not encountered, nor was excessive bleeding a problem. The babies cried spontaneously and none required resuscitation.

Nausea and vomiting occurred in 13 per cent of the cases. It was a troublesome complication when the patient accepted food or fluids during labor. It was encountered early in the series until the fact was recognized. It is advisable to restrict fluids and food during labor. A lowering of blood pressure averaging 10 mm. systolic occurred in 50 per cent of the cases. The reduction was attributed to removal of psychic effects on blood pressure by the pain relief. In the other 50 per cent there was a momentary fall in systolic pressure, sometimes as low a level as 80 mm. Hg shortly after completion of the injection. Recovery was, however, immediate. No therapy other than deep breathing was required. This drop in pressure must not be confused with the hypotension with bradycardia which is frequently seen with spinal anesthesia, particularly in the more extensive blocks. This type of circulatory disturbance was notably absent, save in three cases. In these, the blood pressure dropped to 80 and 90 mm. Hg and remained at this level. It was, however, quickly restored by

centimeter. Lundy and Osterberg,<sup>4</sup> Shannon and Zielinski,<sup>5</sup> and others have reported neither the antibacterial activity effect of penicillin is impaired in the presence of procaine hydrochloride or metycaine, nor is the effect of the anesthetic agent impaired in the presence of penicillin. These encouraging facts prompted the addition of penicillin sodium to the local anesthetic in a series of cases.

### Method

No change was made in intrapartum or postpartum care, suture material, or methods of repair. For 81 consecutive repairs of incisions or lacerations a local infiltration was made of 1 per cent procaine hydrochloride in normal saline to which 250 units of freshly made penicillin sodium were added to each cubic centimeter of the solution. This mixture was made fresh at the time of each delivery.

An average of 45 c.c. was injected into the subcutaneous, intramuscular, and submucosal vulvo-vagino-perineal area by infiltration. In two patients pudendal nerve blocks were effected with 15 c.c. injected bilaterally into Alecock's canal area.

The patients were prepared for delivery by scrubbing the abdominal, pubic, thigh, vulvar, and rectal areas with liquid green soap with the gloved hand followed by removing with sterile water and spraying with merthiolate. Before the repair was done, the towel drapes were replaced, the anal drape was secured with clips, and the gloved hands were washed with green soap.

Postpartum attention to the repair consisted of: douching vulvoperineal area with 1-2000 bichloride of mercury, cotton ball cleansing being used as indicated; spraying twice daily with merthiolate, and applying the vulvar pad which was held in place with a sanitary belt. T-binders were not used.

### Results

Forty-four delivered spontaneously; 31 were delivered by outlet forceps; four were delivered by midforceps extraction; and two were delivered as assisted breech. In the management of these, 49 right mediolateral, two left mediolateral, and 23 median episiotomies were performed. Six patients sustained lacerations of a first or second degree. Thirty patients were repaired with No. 00 chromic catgut suture, 49 with No. 0 chromic catgut suture, and two with No. 1 chromic catgut and dermal sutures. In all but four the skin edges were approximated with a subcuticular stitch.

In 77 the results of the repairs were considered excellent. Three of the four remaining were excellent except for one centimeter shallow separations of the skin only at the distal angle. These separations showed no redness, edema, or slough, and were healed by the fourteenth postpartum day. The fourth repair must be considered less satisfactory, as a large submucosal hematoma developed in the episiotomy area and extended the length of the vagina. The hematoma was evacuated on the seventh postpartum day, and the patient made an uneventful nonmorbidity recovery. The area showed no evidence of infection at any time. These four occurred in right mediolateral episiotomies repaired with No. 0 chromic catgut suture used as a subcuticular stitch.

Associated complications in the puerperium were six cases of mild acute mastitis, two cases of mild endometritis, two postpartum hemorrhages, and one intrapartum hemorrhage from an anterolateral vaginal wall laceration. None of these seemed to influence the course of the repairs. In seven patients there was evidence of extravasation of blood into the submucosal and subcutaneous tissues at the sites of injections. Clinically and subjectively there was no further disturbance. (It was noted this followed the use of one particular manufacturer's penicillin. No further reactions occurred on change to another brand.)

# ADDITION OF PENICILLIN SODIUM TO ANESTHETIC AGENT FOR LOCAL INFILTRATION ANESTHESIA

## Preliminary Report

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**S**ODIUM penicillin is widely used, and its effectiveness in certain conditions and on certain organisms by different methods of administration is becoming more clearly defined. Considerably less attention has been given to its prophylactic use. This is a preliminary report on the addition of 250 Oxford Units of penicillin sodium to each cubic centimeter of anesthetic agent used in local infiltration anesthesia for repairs of incisions and lacerations of the vulvo-vagino-perineal areas sustained during parturition.

In reviewing the first 208 consecutive deliveries of a newly established obstetric department, 169 repairs were made immediately following delivery, of which 116 were under a local infiltration anesthetic and 53 were under an inhalation anesthetic. The results of seven repairs were unsatisfactory (two inhalation, five local). Twenty more were "disturbing" but not unsatisfactory (two inhalation, eighteen local).

The seven unsatisfactory results consisted of: three complete disruptions necessitating secondary repairs, one fistulous tract, and three partial disruptions, the latter causing anatomic and functional defects of the introitus. In two of the complete disruptions there was associated persistent coughing caused by a severe asthmatic attack in one and a partial atelectasis in another. There was no associated pathology in the third. An endometritis of a mild type occurred in two of the partial disruptions.

By "disturbing" results, reference is made to the repair that developed redness and edema within 24 to 48 hours, followed in two or three days by a separation of the skin edges, usually at the outer angle, and frequently extending into the deeper structures, with the sutures noticeably intact. This wound developed some sloughing and sluggish healing which necessitated measures that would encourage the healing from the gutter outward. In these there were no functional defects of the introitus, and anatomic disturbance was slight, if any. There were only three associated conditions such as endometritis, mastitis, and anemia in these twenty cases.

The 169 repairs were analyzed as to location of repair, type of suture used, type of delivery, hours of labor, and associated complications. Beyond the above complications sufficient variation could not be noted to warrant mentioning.

Dissatisfaction over the 27 above mentioned cases prompted investigation along the following lines. Cultures were taken of the sutures, sterile goods, noses and throats of personnel. The technique of the handling of the patient intrapartum and postpartum was reviewed and checked. The methods of repair and handling of tissue were studied. It was reasoned that, because of the edema, redness, and slough with intact suture, there must be a combination of impaired circulation and infection.

To eliminate one factor, infection, the use of penicillin was considered. Bentley<sup>1</sup> reported a 95 per cent primary healing from use of penicillin locally with early secondary suture of flesh wounds. Brown<sup>2</sup> reported much the same results. Lamon and Alexander<sup>3</sup> closed decubitus ulcers and secured primary healing by intramuscular and local injection of 250 units of penicillin per cubic

Further study should include more bacteriologic investigation and probably a variation of dosage, such as 50, 100, 150, and 200 units per cubic centimeter. The addition of penicillin to the local anesthetics used for major and minor vaginal surgery is anticipated.

### Summary

1. Penicillin sodium, 250 units, was added to each cubic centimeter of local anesthetic agent for repairs of lacerations or incisions of the birth canal in 81 cases.

2. Sufficiently encouraging improvement occurred in repairs to urge further study.

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There was some increased discomfort to the actual injection of the local infiltration with the penicillin added solution in about 50 per cent of the cases but this varied with the degree of analgesia and anmesia present. In the remainder of the post-partum course there was not only a general tendency for these patients to have less subjective symptoms referable to the perineum, but objectively the repairs were remarkably free of swelling, redness or discoloration other than described above.

The postpartum checkups at six and twelve weeks clinically presented repair areas of less scar tissue, less tenderness, and more normal elastic properties.

### Comment

Search of medical literature and communications with some outstanding pharmaceutical concerns fail to reveal any previous use of penicillin prophylactically in local anesthetics for obstetric or gynecologic surgery. In the large, well-equipped, adequately staffed maternities, the need for additional protection from infection of repairs possibly does not exist. But the smaller obstetric services of many general hospitals, with minimum facilities and always present personnel problems may find this need.

The site of the surgical field is not only more difficult to prepare, but asepsis is most difficult to maintain in many cases. It is therefore not unreasonable to feel that the repair is potentially infected and that bacteria are being carried into the area with the infiltrating and surgical needles.

Also, some temporary circulatory impairment of the operative area is produced by the chemical and mechanical effects of the local infiltration. This may offer an advantage to pathogenic invading organisms. The penicillin was added to inhibit the bacterial growth during this temporary impairment, i.e., until normal physiologic defense is re-established.

One possible disadvantage in the use of penicillin in this manner is that of sensitizing the patient to further penicillin therapy. If a complication developed that would respond to such therapy, but sensitization prevented its use, a most unfortunate problem might be at hand. However, the seriousness of this potential disadvantage is certainly in a controversial state.

A diversity of reactions to penicillin has been reported, most of which have been systemic effects, whether administered parenterally or locally. Cormia, Jacobsen, and Smith<sup>6</sup> reported serious reactions but no deaths in 0.5 per cent of 2,000 patients treated with penicillin. Jadassohn et al.,<sup>9</sup> Graves, Carpenter, and Uangst<sup>10</sup> further found previous fungus disease and impurities in the brand increased the possibilities of reactions. Welch and Rostenberg<sup>7</sup> reported very low incidence of reactions to crystalline penicillin. However, the mechanism of reactions to penicillin has not been determined.

Only a small percentage of the sensitizations reported follow initial or small doses of penicillin. Lyons<sup>8</sup> claims sensitization is transient and that therapy can usually be continued. Cormia and his associates<sup>6</sup> disagreed. They found the sensitivity to extend for as long as three or more months and that therapy had to be discontinued. None of the patients in this report received further penicillin therapy than that infiltrated. No reactions were encountered other than the seven cases showing subcutaneous extravasation of blood which ceased to occur on change to another manufacturer's product.

Inasmuch as the per cent of reactions to initial administrations of brands free of impurities is small and the clinical results of these repairs are so markedly improved, one cannot help but encourage further study. The gratifying results were obtained in face of increased distressing personnel problems on this service.



comparable to the following observations, although one important factor, loss of fertility, is connected with both procedures.

A few psychologic and psychosexual consequences are well known to gynecologists. The removal of a deep-seated tumor might effect anatomic changes which render sexual intercourse less painful, or even make it possible. The relief from manifold distress caused by the fibroid might exert lasting changes in the whole personality. Operations of any type are known to have devastating effect on psychotics. It is not accidental that the neurotic patient's sex behavior shows the most striking changes postoperatively. Sexual perversions appear or disappear, are cured or become unbearable.

All these studies led me to the conviction that neurotic mechanisms, of which frigidity is the most common, are contributory to the growth of fibroids.<sup>8</sup> Paradoxically, it is the case of a woman who was *not* hysterectomized which illustrates this complex problem most clearly. In Julius Bauer's department in Vienna,<sup>9</sup> and, neither before nor after, have I been able to observe a case as strikingly convincing.

CASE 1.—A woman 34 years of age was referred to me ten months after appendectomy (July 17, 1931) with the complaint of diarrhea. The operation had been performed because of severe menometrorrhagia and persistent pains in the appendical region. No anomaly of the genitals could be detected prior to the operation. The patient consented to hysterectomy on the chance that it would reveal some cause for her continuous bleeding.

She was discharged from the surgical ward on the twelfth postoperative day, but was confined to bed for the following nine months, allegedly because of suppuration of a stitch. After that she suffered from diarrhea when she walked aimlessly, although when her walking served any purpose, she felt fine.

This woman alleged that her husband neglected his marital duties to the extent of having intercourse but once or twice a year. She refrained from having extramarital relations only because she feared pregnancy.

Her reaction to the surgical trauma set in when the surgeon told her that her genitals could be saved. She desired castration so that she might indulge in promiscuity without fear of pregnancy. Since the expected hysterectomy was not performed, her first defense against her strong sexual desires diminished her resistance and facilitated the suppuration. When her confinement to bed was eventually terminated, she resorted to diarrhea as another means of defense.

Unfortunately, reactions to operations are not always so easily understood as in this case. Frequently, we observe a behavior for which we hesitate to blame the operation alone. While studying the aftermaths of hysterectomy at Sydenham Hospital, I have seen many a Negro woman who was deserted by her husband when she returned from the hospital. The reason given for the abandonment was that "he had no use for half a woman." I am far from accepting this as an adequate explanation for the husband's behavior, although I do not think this excuse should be disregarded. This brings up the whole question of the reactions on the part of the patient's relatives to the operation and the ensuing repercussions upon the patient herself.

This line of thought, although not strictly belonging to this presentation, explains some observations by no means singular or extraordinary. Psychologists are well acquainted with neurotic manifestations in men after

## PSYCHONEUROTIC SYMPTOMS FOLLOWING HYSTERECTOMY

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**D**URING the past few years I have been strongly impressed by the effects of hysterectomy on neurotics. After surgical intervention some of these women claim that they have new symptoms. There are three outstanding factors about their postoperative reactions.

*First*, even though such a patient is highly intelligent, she does not tell the physician about her "new" symptoms. Indeed, extensive follow-up studies made by critical and experienced gynecologists fail to mention any observation corresponding to the material presented below. Authors who have given meticulous care to hundreds of consecutive hysterectomies are unaware of these changes in their patients' emotional states.

*Second*, the patient has an attitude toward the gynecologist who performed the operation which is different from her attitude toward the psychiatrist to whom she spontaneously presents an abundance of facts which she would never think of telling to the gynecologist. In her reticence toward the operator the patient may impulsively, in accordance with the main patterns of her neurosis, condemn him or protect his reputation.

*Third*, it is my impression that the indication for hysterectomy has an important bearing upon the patient's postoperative reaction. One of my patients who had a hysterectomy for a suspected ovarian malignancy, and another who underwent the same operation for a perforation of the uterus during abortion, showed effects different from those manifested by neurotics in whom the uterus was totally or subtotally removed for fibroids. In the past three years I have seen 32 patients who have undergone hysterectomy for fibroids, but only six of them believed that their neuroses became more severe after the operation. Two reported that hysterectomy had favorably affected their neuroses. One of the latter was freed from her alcoholism and sexual promiscuity, apparently by the termination of her premenstrual tension. This patient, however, went to extremes of chastity, and some oral trends of her neurosis became predominant. She is now being treated, and therefore her anamnestic statements are reported without further comment.

The psychiatrist presents the results of genital operations in a way different from the gynecologist. A. J. Lewis and J. Jackson,<sup>1</sup> who studied 67 women, mention only a short episode of insanity in a previously normal woman after cesarean section and subtotal hysterectomy. States of transitory confusion have nothing to do with the manifestations in question. The investigations of B. Milt<sup>2</sup> and Hans Binder,<sup>3</sup> who noted the effects of sterilization by partial resection of the tubes, have stated the potential dangers of this procedure which, in contradistinction to hysterectomy, fails to disturb the physiologic functions of the genital apparatus. These studies, however, contain not a single report

against the restrictions imposed by her mother's frailty. However, all the patient's expressions of hostility followed a pattern of childhood, when she reasoned like this: "If my mother succeeded in marrying my father, why shouldn't I be able to do the same?"

The conflict between the "I" and the "She" was fought on different battlefields. One was the patient's body; she constantly depreciated her own appearance and harbored a tremendous shame about her genitals. Another battleground was the patient's eyes, which became a symbol expressed by the phonetic identity between "I" and "Eye." The patient was convinced that her vision would eventually succumb to a glaucoma, and had seen an ophthalmologist. With her usual ambivalence, she misconstrued his diagnosis and assumed that he predicted blindness when he had actually told her that her eyes showed no deterioration. This is further evidence of her hostility toward the "I," i.e., herself.

CASE 3.—A white woman, married, childless, 30 years of age, was referred to the psychiatric clinic of Beth Israel Hospital in the spring of 1944 for obsessions. She gave the following history: In December, 1943, she consulted her family physician, complaining of pain in the left lower quadrant and frequency of urination of a week's duration. She was referred to the Bronx Hospital where subtotal hysterectomy was performed on her. Both before and after the operation, the patient showed great concern about her fertility. When after persistent inquiry she learned that the operation had left her sterile, she became deeply depressed, neglected herself, and gave utterance to suicidal ideas.

At this point, her sister-in-law stepped in and assumed the role of the psychotherapist, insisting that the sick woman "was keeping something from her mind." At her prompting, the patient confessed to an alleged rape by an older boy when she was five; and to her habit, at the same age, of "playing house" with one of her brothers. These confessions intensified the depression. At that time, she was given a series of seventeen electro shocks which relieved her depression, but subsequently, obsessions took possession of her, being heard incessantly, whenever the patient was idle. One phrase: "Why did I tell it to Judy?" (her sister-in-law) disappeared under observation and was replaced by: "I'm going to destroy myself."

When the patient was giving her history, she stated: "In the back of my mind I asked myself, why should I have this tumor?" Her own explanation was that five years prior to hysterectomy she met with a slight auto accident, in which her back bumped against the ceiling of the car and, simultaneously, she perceived "kind of sexual sensation in the womb." About three years prior to hysterectomy, a lipoma was removed from the very spot where she bumped her back. The patient believed that the tumor of the back and of the uterus were both caused by the insignificant accident.

Further details of her history led us to assume that this accident might have a deeper meaning to the patient. Supporting this assumption was the fact that twelve years before her operation, the brother with whom she had "played house" was accidentally drowned when the taxi in which he was riding was driven into a river.

This brother's role in the patient's life was revealed in sodium amytal hypnosis. To quote the patient: "The reason why he died so young was he slept with me in the same bed. Besides, he picked up my dress, examined me here and there. He used to inject something in me. A little girl of five does not experience anything. Then our mother was sick and it is natural that he examined me. We both could not live, that's why he died. Maybe God punished my brother. After my marriage, I had the feeling that if he were alive I would be in an awkward situation."

gynecologic operations performed upon their wives. The most common outcome is impotency. In these cases the woman's real castration is misinterpreted as a menace to the male, either a symbolic realization of death wishes against the wife, or as a safeguard against his intention of abandoning her. The phobia of a girl was centered around her mother's gynecologic operation which was performed fifteen years prior to the manifestation of the phobia. The actual reason for disclosure of this phobia was the first intercourse which symbolized the daughter's full identification with her mother.

These observations illustrate some of the complications inherent in this kind of surgery. It goes without saying that the surgeon cannot be blamed for this outcome.

CASE 2.—A white professional woman, unmarried and virginal, 46 years old, complained of uncontrollable crying spells, of a feeling of inferiority and inadequacy, or impaired sleep and failing memory. These symptoms became so severe that she was afraid of becoming completely incapacitated for her work. In the first psychologic interview, in the spring of 1944, she alleged that these symptoms began after hysterectomy performed on her in the fall of 1940. This statement was corroborated by investigation. The indications for the operation were a fibroid uterus up to the umbilicus; severe uterine hemorrhages which lasted for four years prior to the operation and caused severe anemia; and gastric, cardiac, and urinary distress. The latter manifestations were completely relieved by the surgical procedure.

There was no immediate abnormal reaction to the operation. Relieved from her manifold pains, the patient failed to notice any unpleasant aftermath as long as she stayed in the hospital. However, her strength and endurance returned slowly. A long period of inertia followed her return home and the patient noticed a steady increase in nervousness. She became afraid of losing her job, of being looked at. She was filled with a sensation of hollowness which forced her to lie down often, and to sit on the curb when she waited for a bus. She had the feeling that she had been "turned inside out."

Four months after the operation she resumed her normal activities, although hampered by the symptoms just described, symptoms which slowly gained momentum.

The patient stated that her crying spells were quite involuntary. She attributed them to recurring dialogues between "I" and "She" which were carried on according to the following pattern: "I" asked watchfully and objectively, "How does 'She' feel?" "She" responded first with consternation, then with anxiety and tenseness. "She" longed to get help from someone, but according to an iron rule which dominated the patient's existence, it was necessary to hide the need for help behind the opposite type of behavior. At first the crying spells ceased in another person's presence; however, later they became apparent in one way or another.

Further investigation showed that the "I" constantly tormented and frightened the "She." During treatment the patient once related the discovery of a lump in her breast. The "I" had forbidden her to seek help, although the patient was terrified at the thought that it might be a breast cancer. Fortunately, the tumor was found to be benign.

The relationship between the "I" and the "She" was found to exemplify the patient's antagonistic relationship to her mother. "She" was the mother; "I" was the patient who had nursed her mother during a sickness of many years' duration and yet was unmoved when the mother died. The daughter belittled her mother's intelligence, was ashamed of her poor English, and revolted

incision, the portion to be removed, especially and persistently about the fec; she wishes to be informed about the time needed for operation and convalescence, kind of anesthesia, and many other details of lesser importance.

Their wish to save fertility stems from the craving to compete with men, as shown in their professional career and conduct of marriage. These women were classified by K. Abraham<sup>1</sup> as the revengeful type, and the next victim is the operator whom she charges with neglect, incompetence, or selfishness. These patients will accuse the operator of having ruined her health, they will make him responsible for having caused her menopausal symptoms, even many years after the operation.

The last case report illustrates this type in which psychotherapy is instrumental in changing this disastrous attitude thoroughly by presenting the patient with its predominant trends. The symbolic meaning of a child of her own, delivery, or pregnancy, is self-evident in the case presented and is similar in other patients. One has to keep in mind that the symbol child is usually replaced by other objects, for instance, by a social position, professional career, finally, by the choice of the sexual object.

*The Masochistic Woman.*—This type has been discussed widely in the literature in which monstrous examples are recorded. Grünert<sup>4</sup> described a woman 39 years of age who was operated upon for adhesions four times a year with a total of twenty-six laparotomies; and Drescher<sup>3</sup> reported on a 23-year-old girl with a record of seven different operations within less than two years. Krönig referred to the *furor operativus passivus* of this type. I would like to group my first case in this class, although her appendectomy was her only operation. I am convinced that a woman of her type will find reasons for numerous operations, and also surgeons willing to perform them.

It must suffice to suggest that this type should be treated psychologically at the earliest convenience, that the operation be postponed (of course, only if circumstances allow) until the psychological preparation has yielded some results. The prognosis is, generally speaking, excellent.

### Conclusions

The closing words of my presentation aim to forestall criticism on the surgeon's part. The discussion of this postoperative complication merely stresses the fact that castration for uterine fibroids is likely to elicit untoward neurotic reactions, which are less due to surgery itself than to some psychodynamics which, in my opinion, are acting upon myofibroids in one way or another. This investigation strives for the elimination of one factor which might abate the results of surgery.

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Through the use of sodium amytal, it could be shown that the patient never ceased to feel guilty for her promiscuous sex life at the age of five, that she had expressed death wishes against her brother, that the only means of atoning for her misdeeds was having a child. When the hysterectomy rendered this prospect impossible, the patient resorted to depressions, the masochistic character and function of which are obvious. When the depression was alleviated by the electro shocks, the obsessional ideas served the same purpose.

This observation shows the specificity of the hysterectomy. The removal of the lipoma had no effects on this patient's conflicts because this tumor had no emotional connection with the infantile trauma. However, the operation on the sex region destroyed the equilibrium between guilt and expiation.

It is not by chance that both tumors were connected with an auto accident and that her brother succumbed to a similar cause. This similarity of both episodes was apparently accepted by the patient's unconscious as a retaliation for her death wishes against her brother. In any case, the details presented explain the patient's frigidity and the latter, in turn, enhances the growth of fibroids, according to E. Kehrer's theory.<sup>5</sup> I would like to add that many women afflicted with fibroids give similar histories.

The observations just presented permit a few statements pertinent to the performance of this operation in neurotic women. First, castration may precipitate a serious psychic trauma. This aspect has been documented extensively. Second, this study shows that there is opportunity to prevent this ill effect. We may group neurotic women, about to undergo this operation, in three categories: The indifferent, the overanxious, and the masochistic. This subdivision, I believe, can be made by every physician, even without deeper psychologic training.

*The Indifferent Woman.*—She may accept the prospect of hysterectomy with no apparent fear or apprehension. She usually fails to have its necessity verified by other physicians. It is this type who almost idolizes the physician who performed the operation, who bears willingly and submissively all restrictions, who pays, without the slightest hesitation, any fee requested. On the other hand, she will minimize the seriousness of her symptoms, thus seeking help as late as possible. In other words, she establishes a strong positive transference to the physician, thus reviving her old relationship to her father. That was clearly shown in the second case report in which a woman's castration complex is expressed in the wish fulfillment type, according to K. Abraham.<sup>1</sup> The main complaint of this patient was that castration had rendered life worthless to her, preventing her from further fantasies.

So far as this type is concerned, I must admit the difficulty, even impossibility of predicting this outcome. This patient had been operated on by an outstanding gynecologist who was renowned for his interest and activity in psychoanalysis. Behind a submissive facade and a ladylike attitude, this patient concealed her neurosis, and she revealed it only when she was faced with complete destruction. She was afraid to hurt her doctor's reputation and confide in him the deterioration of her neurosis subsequent to his indispensable surgery.

*The Overanxious Woman.*—This woman will turn to numerous other authorities for re-examination and re-consideration of the necessity of the proposed surgery. She might insist that only the tumor be removed and that otherwise her genitals be kept intact—an insistence apparently exaggerated if the patient is single, virginal, and close to the menopause. She simply cannot give herself in any physician's hand, she impulsively bargains about the site of the

TABLE I

	PATIENTS RECEIVING DEMEROL AND HYOSCINE 1 HOUR OR LESS BEFORE DELIVERY	PATIENTS RECEIVING DEMEROL AND HYOSCINE MORE THAN 1 HOUR BEFORE DELIVERY
Rate of respiration		
Range	28 to 78/min.	24 to 64/min.
Average	44.9/min.	43.7/min.
Average depth of inspiration		
Range	11.26 to 31.23 c.c.	15.38 to 26.23 c.c.
Average	20.19 c.c.	19.98 c.c.
Minute volume of inspired air		
Range	459.69 to 1,593.14 c.c.	464.31 to 1,390.62 c.c.
Average	887.03 c.c.	874.44 c.c.
Minute volume per pound body weight		
Range	59.9 to 212.7 c.c.	64.9 to 188.1 c.c.
Average	128.02 c.c.	120.98 c.c.

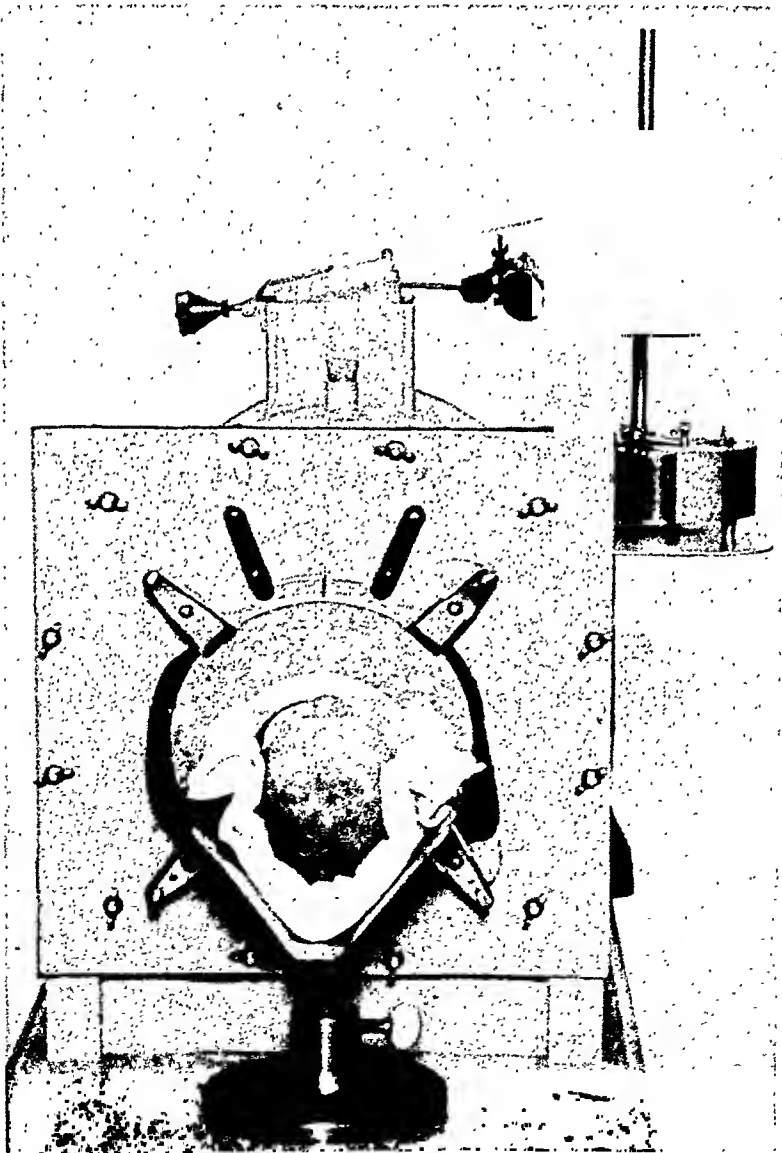


Fig. 1.—Photograph of equipment used in this study. Reprinted with the permission of Dr. A. H. Washburn.



# RESPIRATION DURING THE FIRST HOUR OF LIFE

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SINCE demerol was synthesized in 1939 by Eisleb and Schaumann, there have been many reports of its effective use and pharmacologic action. The purpose of this study was to determine if the use of demerol and hyoscine during labor exerted any action on the respiration of the newborn infant, when given in dosages recommended by Roby and Schumann;<sup>1</sup> and also to obtain accurate information on the respiration of the newborn from the time of birth to one hour of age.

The equipment used in carrying out this study is the same as that developed and used by Deming and Washburn<sup>2</sup> in their report, "Respiration in Infancy." Records were obtained by an indirect method. The newborn's body was placed in an air-tight cylinder with the head outside of the chamber. A circular rubber collar was used to make an air-tight seal around the infant's neck. A spirometer was connected with the air-tight cylinder, and a writing point was attached to the spirometer float. Recordings were made on a kymograph. Inspiration was represented by upstrokes on the records, and expiration by downstrokes.

## Results

A total of 68 records of respiration in 40 infants during their first hour of life were obtained. The earliest records were obtained on two infants seven minutes of age. Eighteen records were obtained between 10 and 15 minutes of age, 23 records between 16 and 30 minutes, 14 records between 31 and 45 minutes, and 11 records between 46 and 60 minutes of age. All records obtained were on full-term normal infants, and none of the recordings were made while the infants were crying. All but two newborns in this group were delivered vaginally. These two infants were delivered by cesarean section after eight- and nine-hour tests of labor for borderline cephalopelvic disproportion. These two cases were not separated from the others in the statistical analysis because of their similarity to the other cases.

Fifty-three records were obtained on 31 newborns whose mothers had received demerol and hyoscine. The minimum dosage was 100 mg. of demerol and 0.6 mg. of hyoscine. The maximum dosage given was 300 mg. of demerol and 1.5 mg. of hyoscine during a nine-hour period before delivery. In two instances the medication was given intravenously ten minutes before delivery. Seventeen of the patients received demerol and hyoscine one hour or less prior to delivery. Thirty-one records were obtained on these 17 patients. Twenty-two records were made on 14 patients who received the medication over one hour before delivery. An analysis of these records appears in Table I.

From Table I it can be seen that the time of administration of demerol and hyoscine prior to delivery exerts little or no effect on the newborn baby's respiration.

In Table II a comparison of the 53 records obtained on cases receiving demerol and hyoscine is made with the 15 records in 9 cases not receiving any medication.



TABLE II

	PATIENTS RECEIVING DEMEROL AND HYOSCINE	PATIENTS NOT RECEIVING DEMEROL AND HYOSCINE
Rate of respiration		
Range	24 to 78/min.	24 to 66/min.
Average	44.4/min.	48/min.
Average depth of inspiration		
Range	11.26 to 31.23 c.c.	13.03 to 38.40 c.c.
Average	20.10 c.c.	17.16 c.c.
Minute volume of inspired air		
Range	459.69 to 1,593.14 c.c.	455.07 to 1,769.46 c.c.
Average	880.53 c.c.	810.17 c.c.
Minute volume per pound body weight		
Range	59.9 to 212.7 c.c.	78.8 to 247.4 c.c.
Average	124.9 c.c.	121.66 c.c.

### Comment

From this tabulation one can conclude that demerol and hyoscine definitely exert no effect on the respiration of the newborn. Therefore, when abnormalities occur in the respiration of the newborn after demerol and hyoscine medication, the etiology must be explained on some basis other than the medication.

In all but one case the infants cried within a few seconds of delivery and no resuscitation was required. Resuscitation was necessary in the one case of a persistent occiput posterior. This study would undoubtedly have been more interesting if records could have been obtained before 7 minutes of age. This was impossible because of the technical difficulties of placing and sealing the infant in the chamber. Even though most of the effects of a general anesthetic on the newborn have disappeared after seven minutes, it was deemed advisable to make a comparison between the respiration of those infants born from mothers receiving a general anesthetic with those born from mothers not receiving a general anesthetic. There were 21 cases in this series delivered while the mother was receiving a general anesthetic (ether or cyclopropane). The other cases, in most instances, were delivered with the aid of a pudendal block. Those cases receiving a general anesthetic received only oxygen just prior to the delivery of the head and during delivery of the body, never allowing the anesthetic to become so light that the patient became restless. There is no doubt that an incorrectly administered general anesthetic does exert a definite influence on the newborn's respiration; however, this was not noted in our cases. The minute volume per pound body weight is used for comparison, since we feel this is the most accurate basis for comparison of respiration in the newborn. In 37 records on the 21 patients receiving a general anesthetic the minute volume per pound body weight was 124.28 c.c.; whereas, in the 31 records on the 19 patients not receiving a general anesthetic, it was 124.08 c.c. Therefore, we conclude that the general anesthetic exerted no effect on the infants' respiration after 7 minutes of age.

A comparison was also made in the minute volume per pound body weight in relation to the parity of the mother. The 14 babies delivered from multiparous mothers had a minute volume per pound of 134.2 c.c.; whereas, the value for the 26 babies delivered from primiparous mothers was 117.8 c.c. Even

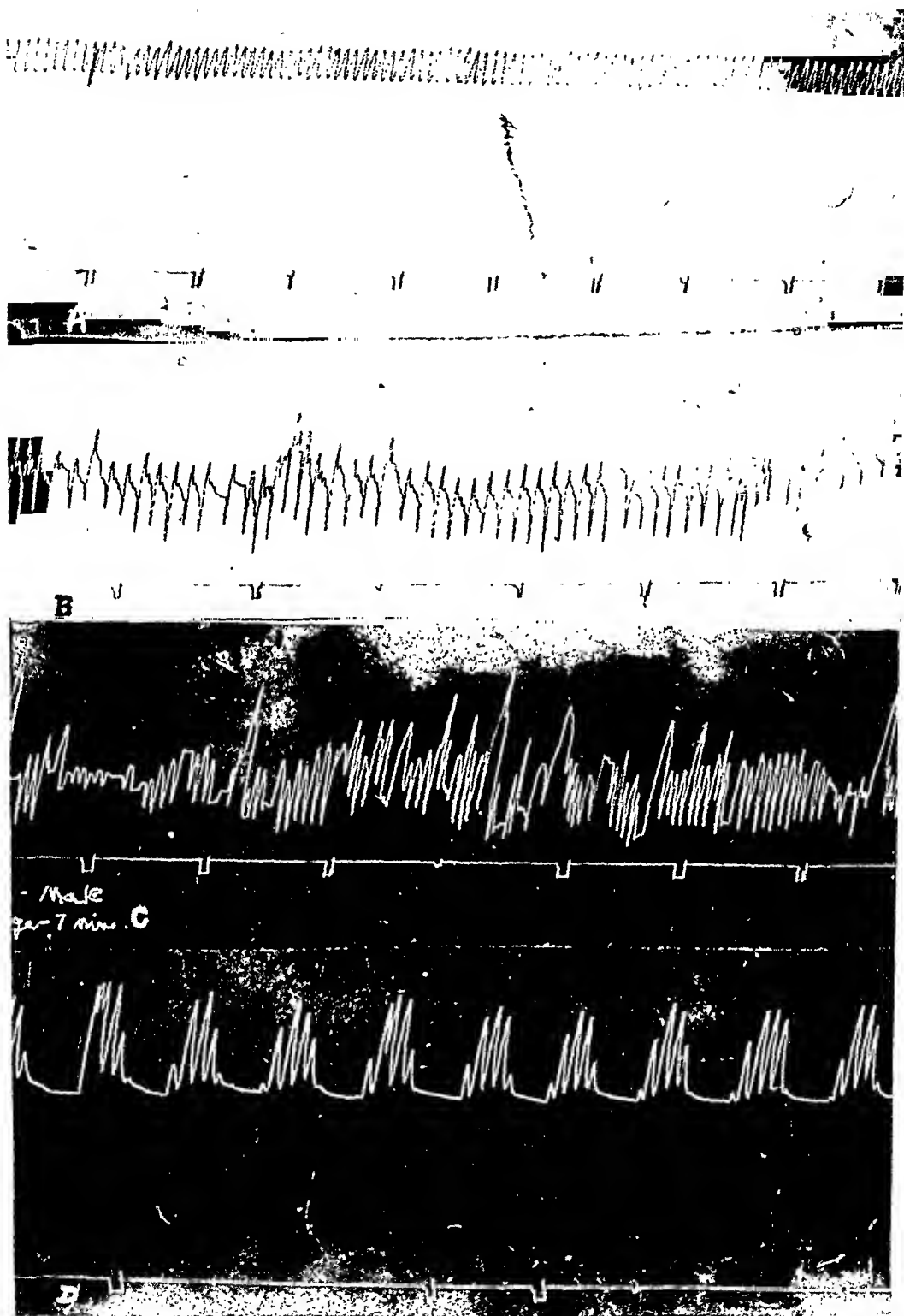


Fig. 2.—A, Example of regular type of respiration obtained on an infant 15 minutes after birth.

B, Example of cog-wheel expiration obtained on an infant 25 minutes old.

C, Example of irregular type of respiration obtained on an infant 7 minutes old.

D, Example of extremely periodic type of respiration obtained on an infant 3 days old. Note the fine excursions that occur during the apneic portion of the record due to heart action.

The author is greatly indebted to Dr. A. H. Washburn for the use of the equipment which made this study possible, and to Dr. C. B. Ingraham and Dr. Richard Whitehead for their numerous helpful suggestions.

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though this is a small series of cases, we believe that a difference of 16.4 c.e. per pound body weight is great enough to be of significance.

In summarizing our records to obtain values for respiration in infants one hour of age or less, it was felt that all 68 records should be included, since no evidence of any effect of either the medication or the anesthetic could be found in the previous analysis. A comparison is presented with the values obtained by Deming and Hanner<sup>3</sup> for infants during their first day of life.

TABLE III

AVERAGE RATE PER MINUTE		AVERAGE DEPTH OF INSPIRATION PER C.C.	AVERAGE VOLUME PER MINUTE, C.C.	AVERAGE VOLUME PER POUND, PER MINUTE, C.C.
Our results	45	19.43 c.c.	861.5 c.c.	124.1 c.c.
Deming and Hanner	41	18.70 c.c.	734.0 c.c.	106.1 c.c.

In all instances our values for the infant one hour of age or less are higher than the values reported by Deming and Hanner for infants during their first day of life. Their results are very similar to values we obtained on six infants later during the first day of life. Therefore, we feel justified in concluding that the volume of air inspired per minute per pound body weight is higher during the first hour following delivery than later during the first day of life.

No attempt was made to divide the records into types of breathing; however, it is of interest that all but one of the types described by Washburn and Deming were noted. The periodic (Cheyne-Stokes) type of respiration they describe was not obtained on any of the infants one hour of age or less, but was obtained on a normal female infant three days of age. Photographs of the types observed are included (Fig. 2). The record obtained on the 3-day-old infant is included to illustrate the accuracy of the equipment used. In the apneic portion of this record, the infant's heartbeat is recorded.

### Summary

1. Analysis of 68 records of respiration in the newborn one hour of age or less is presented.

2. From this study it has definitely been shown that demerol and hyoscine, no matter when administered, exert no effect on the respiration of the newborn from 7 minutes to one hour of age. This had been accepted as a clinical fact; however, prior to this time, no accurate assay has been presented.

3. It has been shown that a general anesthetic, when it is properly administered, exerts no effect on the respiration of the newborn after 7 minutes of age.

4. During the first hour of life infants born of primiparous mothers had a lower respiratory volume per pound body weight than those born of multiparous mothers.

5. The volume of air inspired per minute per pound body weight is greater during the first hour following delivery than later during the first day of life.

6. Values are presented which can be used as normal values for respiration in the very young infant.

4. On the fourth day (ninety to one hundred hours post partum), in addition to the abdominal exercises which were continued daily, the twice daily use of the knee-chest position (without spreading the buttocks) for two minutes was begun. The patient spent thirty minutes in a chair in the morning (while the bed was being made) and, if the response was good, was allowed to eat her evening meal sitting up at a card table.

5. She was allowed up and about twice for thirty minutes each time on the fifth day and, if she had a private room, was given toilet privileges.

6. On the sixth day all patients were given toilet privileges and permitted three one-hour periods out of bed. She was instructed in perineal care and practiced it herself.

7. On the seventh day the patient was permitted to take a shower and spend half the hours of the day up. Because of the nursing shortage she was encouraged to make her own bed. She ate all her meals at a table, and received instruction in the nursery.

8. On the eighth day she was allowed to wash her hair herself, and was encouraged to walk through the corridors of the wing. If she desired to go home, or if there was a shortage of beds, she was discharged.

9. Her instructions included the continuation of the abdominal and knee-chest exercises, and the addition over the next two weeks of others involving the leg, abdomen, and flank muscles. She was permitted to go up and down stairs cautiously and with limitations that varied with the circumstances. Douches were begun with the appearance of lochia alba. The patient was advised to be gradual in her resumption of work, and in a few cases was allowed to travel, even across the country, when the baby was three weeks old.

No harmful effects were noted as long as five months post partum. On the contrary, the benefits of this regimen were striking. The women consistently had a high morale and a sense of well-being, and multiparas compared their status daily with that of the previous pregnancies with actual enthusiasm.

The degree of involution of the uterus was not recorded, but the impression remains that it was faster than usual. The lochia was more profuse the first three days, despite the exhibition of oral ergonovine. In only 17 cases was true lochia rubra noted on discharge from the hospital, and in only one did it persist for three weeks. Retained secundines were extracted in two cases of subinvolution at the hospital, and in a third case a roll of secundines was withdrawn at the six-week visit, there being, however, no bleeding during the interval. One woman developed a severe uterine hemorrhage on the eighth day, the cause being undetermined, but, as she had had an identical episode with her first pregnancy during which she had been in bed for seven days post-partum, it was deemed irrelevant to the early rising.

Episiotomies were repaired with No. 0 plain catgut in layers, subcuticularly for the skin. In three cases there was separation that included the muscle layers. One woman weighed 286 lbs., and tissue healing under the best circumstances would have been difficult; the second woman had a frank infection of the episiotomy area before the separation, and it is questionable what part activity played; in the third case no specific cause was assignable. But the percentage of separations was not significantly greater than is found in ordinary cases.

There were no frank pelvic infections, and during the hospital stay only five cases of true morbidity were recorded (100.4° F., lasting two or more

## EARLY PUERPERAL RISING\*

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**S**TIMULATED by the success which has attended the early ambulation of general surgical patients, a study was undertaken of the effects of similar treatment on women immediately after childbirth. The careful basic work of Bernard Newburger,<sup>1</sup> published posthumously in 1943, showed that in experimental rats postoperative activity accelerated the early phase of healing of incised tissues, and it was felt that the physiology of the pregnant and parturient woman did not differ sufficiently from that of other surgical conditions to anticipate a less favorable result than that obtained either in experimental animals or human surgical cases.

A total of 221 women were studied between December, 1944, and December, 1945, at the Regional Hospital, Fort Knox, Kentucky; McCaw General Hospital, Walla, Walla, Washington; and Bushnell General Hospital, Brigham City, Utah. The need for early postpartal activity came about both because of the shortage of beds allotted in Army hospitals to dependents of officers and men in the service, and the necessity on the part of the young wives of reducing to a minimum the period of invalidism following their deliveries. These girls lived near Army posts far from mothers and relatives who might help them on their discharge from the hospital, and home nursing help, either trained or practical, as well as domestic help, was almost impossible to obtain. Their living conditions were often substandard, and most of the young mothers lived in constant expectation of sudden changes in station or overseas' orders for their husbands. Thus, almost the entire group was impelled by circumstances to forego the luxury of ten days in the hospital and three more weeks of semi-invalid care and consideration as convalescents.

At first the cases for early rising were selected, but because of the encouraging results, a routine was gradually developed which was used on all uncomplicated parturitions. The exceptions included any general medical or surgical condition, toxemia, severe anemia, the loss of over 500 c.c. of blood at the time of delivery, and any unusual circumstances of labor that offered potentialities of infection. The use of forceps and episiotomy, which was almost routine, was not a contraindication. The procedure consisted of:

1. Standing, assisted, by the side of the bed for one full minute within the first twenty-four hours after delivery. The patient was allowed to lie on her abdomen as desired, and a full diet was offered to her.

2. On the second day she sat on a chair for five minutes.

3. On the third day (a) the patient sat up in a chair some distance from the bed, and to which she walked for five minutes twice during the day; (b) abdominal exercises in bed were started, consisting of tensing the abdomen and alternately raising and lowering the head and shoulders (unassisted by the arms) to the easily tolerated height, ten times, 3 to 5 times a day.

\*Presented at a meeting of the Cincinnati Obstetrical Society, May 16, 1946.

sense of well-being and are benefited psychologically not only during the puerperium, but in their attitude toward the entire episode of pregnancy. They are prepared by the regimen of increasing activity to leave the hospital by the eighth day post partum, and their convalescence at home is shortened considerably.

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days). One was the infected episiotomy, and one was accompanied by such terrific breast engorgement as to leave no doubt as to the cause. The other three represented low grade infections of the lochiametra type. Again, this incidence represented no increase in morbidity that might be ascribed to early rising.

One woman only had any symptoms that might conceivably have indicated thrombophlebitis, but she had no fever. The routine was interrupted in her case, keeping her in bed; after three days, during which her symptoms disappeared, she was allowed up and was discharged on the tenth day.

Lactation seemed to be unaffected by the early activity, although no specific studies were made. An unusually large number of these mothers preferred not to nurse, and lactation was suppressed easily with estrogenic substance.

Unfortunately, only 140 of these 221 patients reported for examination six weeks post partum. Among these women, 23 had a uterus that was definitely retroverted (third degree), and another eight were described as having first or second degree retroversion. This is at most 26 per cent, which compares favorably with the 40 per cent of women ordinarily conceded to have retroversion at the six-week visit. There were no cases of descent and no sequelae of childbirth that might be ascribed to straining of the ligaments or failure to rest the heavy puerperal uterus. This is to be expected, inasmuch as recumbency allows gravity to exercise the least favorable effect on the pelvic organs. While no exact figures are available for comparison, remarkably few women complained of leucorrhea, and only 21 had any cervicitis that warranted comment in the records.

The women were enthusiastic without exception in their report of how they felt during the six-week interval. By the fourth week most of them were doing as much or more than they had done before pregnancy. They felt vigorous and energetic; the comments of the multiparas were of particular satisfaction, regarding not only the physical benefits, but the psychological results.

### Summary

Report is made of the experiences in three Army hospitals with 221 parturitions after which a regimen of early exercise and activity was directed. The routine included standing for one minute the first day post partum, sitting in a chair for five minutes the second day, abdominal exercises in bed, and two five-minute sitting episodes the third day, knee-chest exercises and two thirty-minute sitting periods the fourth day, walking about and toilet privileges on the fifth or sixth day, a shower the seventh day, and discharge from the hospital on the eighth day when desired or necessary.

The incidence of complications, subinvolution, prolonged lochia rubra, episiotomy breakdown, infections, and uterine retroversion was not greater than that found in any series of women treated puerperally with bed rest for six or seven days and hospitalization to the tenth day.

It is felt that early puerperal rising in uncomplicated cases of childbirth is desirable and without danger or unfavorable sequelae. The women have a



TABLE I. INDICATIONS FOR SECTIONS

1. Eclampsia		6
2. Placenta previa		9
3. Previous section		15
4. Cardiac pathology		2
5. Cephalopelvic disproportion		
By x-ray	7	
By trial labor	18	25
6. Elderly primigravida		5
7. Patient's desire		12
8. Abnormal position		7
9. Deformity of mother		2
10. Premature separation of placenta		3
11. Contracted pelvis		14

the placenta. The other two deaths were due to prematurity. The first was a 21-year-old, gravida i, who began to bleed profusely from placenta previa at seven months. The baby survived twelve hours. The other case was a 32-year-old gravida ii who had a previous section. She went into labor prematurely at seven and one-half months, and the baby died fifteen hours after delivery.

Using the standard of the American Committee of Maternal Welfare (temperature 38° C. or over, for two or more consecutive days), our morbidity is 9 per cent. The causes of this morbidity are listed in Table II. Our percentage

TABLE II. CAUSES OF MORBIDITY

1. Endometritis	6
2. Pyelonephritis	2
3. Wound infection	1

compares favorably with figures offered by Smith,<sup>3</sup> 33 per cent; Free,<sup>4</sup> 31 per cent; and Gustafson,<sup>5</sup> 26.6 per cent in elective cases and 53 per cent in emergency cases as compared with Barney et al.,<sup>6</sup> 45 per cent; Briseoe,<sup>8</sup> 23.2 per cent for classical sections, and 9.5 per cent for low cervical operations.

There are certain factors which, we feel, definitely influence morbidity. First, is the type of the operation and the skill of the surgeon. We use a six inch Pfannenstiel type of incision and do a low cervical operation, with suturing of the parietal peritoneum to the uterovesical peritoneum to prevent contamination of the general peritoneal cavity. The uterus is closed in two layers with a continuous suture of chromic catgut No. 1, and a cotton technique is used for the closure of the abdominal wound; cotton No. 40 for anterior sheath of the rectus; cotton No. 70 for subcutaneous tissue and skin.

The second factor is the use of continuous spinal anesthesia for all cases. We use pontocaine and glucose mixture. The continuous method is used so that the smallest possible amount of anesthetic agent may be given, but more is available if needed. We have found no contraindications for the use of this type of anesthesia.

The third factor is good prenatal care. Most of our referring physicians are meticulous concerning this factor.

The fourth factor is the avoidance of postoperative catheterization. Early rising and bathroom privileges obviate this complication. Furmethide is used occasionally when necessary.

## RELATION OF EARLY RISING TO MORBIDITY IN CESAREAN SECTION

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IN 1945 Johnston<sup>1</sup> read a paper before the American Association of Obstetrics and Gynecology in which he stated that in 1923 to 1926 in Houston, Texas, while general surgeons were doing cesarean sections, the maternal mortality was 14.4 per cent. He condemned the operation in the hands of general surgeons. This statement caused us to review our records and compare our standards with those published by other authors as to maternal mortality, fetal mortality, and maternal morbidity. Dieckmann<sup>2</sup> states that maternal mortality should be below 0.5 per cent.

In the period from Jan. 1, 1940, to Jan. 1, 1946, the senior author has performed 207 consecutive cesarean sections without a maternal death. This compared with the figure offered by Johnston<sup>1</sup> of 2.2 per cent; Smith,<sup>3</sup> of 0.9 per cent; Free,<sup>4</sup> of 0.4 per cent; Gustafson,<sup>5</sup> of 0.96 per cent; Barney, et al.,<sup>6</sup> of 1.7 per cent; Rosenson,<sup>7</sup> of 3.2 per cent; Briseoe,<sup>8</sup> of 0.7 per cent; and DeNormandie,<sup>9</sup> of 2.5 per cent.

In Norristown, Pennsylvania, there are no obstetricians who perform cesarean sections. However, there are obstetric chiefs of service who are consulted concerning obstetric practice and emergencies. These men refer the cases to the surgeon for operation. Most of the cesarean sections, therefore, are done on a consultation basis.

From Jan. 1, 1944, to Jan. 1, 1946, 102 cesarean sections were performed by the senior author. The number of hospital deliveries was 2,756, and the total number of cesarean sections by all surgeons was 132, giving an incidence of 4.8 per cent. This is not a true figure, however, because some of our cases are sent from surrounding communities which have hospitals, and many home deliveries are still being done. The indications for this series are outlined in Table I.

In this series our maternal mortality was zero. Our fetal mortality was 5 per cent. Three of these babies were stillborn, and the other two died within twenty-four hours after delivery. The first stillborn was one of twins, in a 17-year-old unmarried Negro girl who had no prenatal care. The fetus was macerated and gave evidence of being dead for a number of days. The other twin was normal and was discharged with the mother. She was admitted as a convulsive eclamptic and was operated upon on the fifth day after admission. The second was a 22-year-old gravida ii, seven months pregnant, who had a premature separation of the placenta. Because of the distance involved in traveling, she was not sectioned until two hours after the onset. The baby was found compressed by a huge clot. The third case was also in a patient with premature separation of

3. Early rising definitely limits the incidence of postpartum and post-operative complications.

4. Early rising leads to considerable economic saving to the patient and allows full use of the available hospital facilities.

5. The patients are grateful not only for lessened expense, but also because of the definite improvement in the postoperative sense of well-being and avoidance of the marked weakness so noticeable in patients kept in bed twelve or fourteen days.

6. The foregoing statistics definitely prove that in the hands of the well-trained general surgeon, the operation of cesarean section can, and is, a safe procedure. The morbidity and mortality can be, and sometimes are, lower in such hands than in those whose work is strictly limited to obstetrics.

Since acceptance of this article for publication, twenty-six cesarean sections were performed; all were ambulatory on the first day with no mortality, and only one patient was morbid for thirty-six hours.

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The fifth factor is an early decision to operate. If the indication is present, the operation should be done before the patient loses strength, and rupture of the membranes or frequent examinations allow opportunity for sepsis to develop.

The sixth and most important factor is early rising postoperatively. We feel that early rising postoperatively definitely lowers the morbidity. During the latter half of 1944, because of favorable reports from various authors<sup>10-14</sup> concerning early rising, we started allowing our patients out of bed on the third postoperative day. Because they did so well, we allowed a few out of bed on the second postoperative day. The results were still more satisfactory, so we routinely allowed all patients out of bed on the first postoperative day. Forty-nine patients were allowed out of bed on the first postoperative day, eleven on the second, and ten on the third. Thus, seventy of our one hundred two cases were out of bed on the third day or before. In this group only two were morbid, a percentage of 2.8 per cent! The first patient was a 24-year-old primipara who was in labor thirty-six hours before we were called. Her temperature was elevated to 101° F., on the second postoperative day, and 101.3° F. on the third day. Following this her temperature returned to normal and remained so.

The second case was a 33-year-old gravida v who was admitted to the hospital in a condition of eclampsia with convulsions. She had concurrently a pyelonephritis with a preoperative temperature ranging between 102° to 104° F. She was delivered of a viable baby and had a normal postoperative course until the sixth day, when the pyelonephritis recurred. This was controlled within a few days.

In this series of 102 cases, there were no cases of thrombophlebitis, phlebotrombosis, upper respiratory infection, pulmonary embolism, cystitis, or wound dehiscence, and only one wound infection. The wound infection occurred in the eclamptic with the macerated fetus. By careful postoperative examination we found no cases of subinvolution of the uterus, prolapse of the uterus, formation of cystocele or rectocele that could in any way be attributed to the fact that the patients were allowed out of bed early. We, therefore, feel that early rising definitely lowers morbidity following cesarean section, and that no complications occurred from its use.

Because our patients are ambulatory and do not develop complications, they are allowed home on the seventh day and eighth day postoperatively. This allows a considerable economic saving to the patient and gives a quicker hospital turnover, allowing full use of the available hospital facilities.

### Summary

1. Two hundred seven cesarean sections were presented with the maternal mortality of 0. One hundred two consecutive cases are reported with a fetal mortality of 5 per cent, and maternal morbidity of 9 per cent. In cases in which patients were allowed out of bed early, the morbidity was only 2.8 per cent.

2. No complications developed from the routine practice of getting all patients out of bed on the first postoperative day.

TABLE I. THE LIPID DISTRIBUTION IN NINE HUMAN PLACENTAS\*

SUBJECT	TOTAL LIPID	NEUTRAL FAT	ESSENTIAL LIPID†					PHOSPHOLIPID			
			TOTAL	CEREBRO-SIDES	FREE CHOLESTEROL	CHOLESTEROL ESTERS	TOTAL CHOLESTEROL	TOTAL	CEPHALIN	LECITHIN	SPHINGO-MYELIN
L. F.	13.41	3.89	9.52	0.40	0.95	0.67	1.35	7.50	2.30	4.29	0.91
V. G.	12.92	3.99	8.93	0.62	1.00	0.53	1.32	6.78	1.92	3.69	1.17
V. K.	11.66	2.63	9.03	0.98	1.09	0.31	1.28	6.65	2.47	3.04	1.14
V. L.	12.73	3.84	8.89	0.29	1.06	0.49	1.35	7.05	2.54	3.43	1.08
J. M.	10.97	2.16	8.81	0.29	1.05	0.52	1.36	6.95	2.25	3.75	0.95
D. M.	11.21	2.15	9.06	0.76	0.89	0.79	1.36	6.62	2.70	3.04	0.88
C. O.	16.75	7.75	9.00	0.32	0.95	0.44	1.21	7.29	3.34	2.95	1.00
V. S.	11.94	2.57	9.37	0.90	0.99	0.66	1.38	6.82	1.47	4.40	0.95
A. S.	9.61	2.59	7.02	0.18	0.89	0.48	1.17	5.47	1.36	3.33	0.78
Average	12.36	3.51	8.85	0.53	0.99	0.54	1.31	6.79	2.26	3.55	0.98

\*Values are percentages of dry weight.

†Essential lipid includes phospholipid.

# COMPOSITION OF THE HUMAN PLACENTA

## II. Lipid Content

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LIPIDS are important sources of nourishment for the growing fetus and, with the improved methods of analysis, it has been possible to determine the partition of the various lipid fractions in the tissue of placentas delivered following the birth of normal infants at full term.

Klaus<sup>1</sup> emphasized that methods of preparing the tissue and the selection and use of solvents in the extraction process explain the diverse results present in the literature on the lipid content of the human placenta. Higuchi<sup>2</sup> found in full-term human placentas 0.85 Gm. of fatty acids per 100 Gm. of fresh weight, but if the placentas were thoroughly washed, only 0.54 Gm. per 100 Gm. was found, indicating that one-third of the first value was from the blood present. Klaus drew attention to the comparatively low values for lipid phosphorus which Bienenfeld<sup>3</sup> obtained, attributing them to the use of petroleum ether as an extraction solvent. The special value of Bienenfeld's work lay in her early demonstration of the reduction of lipids in the human placenta during pregnancy. Her comparison of placentas from pregnancies of three to five months with placentas at term indicated a decrease in total petroleum ether extract from 8.6 to 4.4 per cent of the dry weight. Total cholesterol dropped from 2.25 to 0.37 per cent of the dry weight and cholesterol esters from 1.25 to 0.12 per cent, thus the free cholesterol diminished less than did the cholesterol esters.

Watanabe,<sup>4</sup> in the developing human placenta, demonstrated a fall in total cholesterol, total ether-soluble phosphorus, total lipids, and total fatty acids. Needham<sup>5</sup> pointed out that Watanabe's data definitely brought into focus the question of the source of fetal food: whether the placenta elaborates and stores nutriments or whether the fetus draws from the maternal blood as needed. Watanabe's lipid data, expressed in terms of weight of the embryo, show that at the fourth month of development the fats and lipids of the placenta are present in greater quantity in relation to the weight of the embryo than at any other time. From these results Needham points out a similarity between the developing placenta and the developing hen's egg. In both there is disintegration of the lipid, releasing fatty acids, phosphorus, and choline.

Evidence of important nutritional functions of the placenta have been contributed by Boyd and Wilson,<sup>6</sup> who, in experimental studies on the transfer of nutriments through the umbilical vein to the human fetus, have demonstrated the passage of phospholipids, free cholesterol, and cholesterol esters.

### Procedure

The lipid distribution was determined in placentas obtained following delivery of nine healthy women at full term.\* The preparation and drying of the material are described in the preceding paper.<sup>7</sup> The dried material was extracted with hot ethanol, then with ethyl ether. The final extracts, combined, represented approximately a three to one mixture of alcohol and ether,

lipid contents of the guinea pig placenta. With the exception of neutral fat, his work shows a different lipid pattern from that in the human placentas reported here. In the guinea pig free cholesterol and phospholipid are double, and ester cholesterol one-half that found in human placentas.

Table II summarizes the lipid pattern of the placentas. Of the total lipid, two-thirds was essential lipid (total lipid minus neutral fat). The largest component of the essential lipid, approximately three-fourths, was phospholipid, with free cholesterol comprising 11 per cent, and cerebrosides and cholesterol esters each 6 per cent. Of the phospholipid, one-half was lecithin, one-third was cephalin, and 14 per cent was sphingomyelin.

### Summary

The total lipid (phospholipid [cephalin, lecithin and sphingomyelin] free and combined cholesterol, cerebrosides and neutral fat) distribution in nine human placentas is reported. No great individual variations in the lipid pattern were noted. Of the total lipid, one-fourth was neutral fat. Phospholipid comprised three-quarters of the essential lipid (total lipid minus neutral fat); and of the phospholipid content, one-half was lecithin, one-third was cephalin, and 14 per cent was sphingomyelin.

The total lipid averaged 12.36 per cent of the dry weight, of which 3.51 per cent was neutral fat and 8.85 per cent was essential lipid. Of the dry weight, 0.53 per cent was cerebrosides, 0.99 per cent was free cholesterol, 0.54 per cent was cholesterol esters, and 6.79 per cent was phospholipid. Cephalin averaged 2.26 per cent of the dry weight of the placentas, lecithin was 3.55 per cent, and sphingomyelin was 0.98 per cent.

NOTE.—The third contribution, dealing with the vitamin content of the human placenta, will be included in the next issue.

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and were analyzed for sphingomyelin, total and free cholesterol, galactose, and acetone-soluble glycerol. From the analyses, total phospholipid, choline phospholipid, cephalin, lecithin, cholesterol ester, cerebrosides, and neutral fat were calculated. The complete details of all methods used for analyses have been published.<sup>8</sup>

### Results

The lipid composition of each of the placentas is presented in Table 1. The total lipid averaged 12.36 per cent of the dry weight, and neutral fat, 3.51 per cent. Bienenfeld obtained a total lipid value of 4.4 per cent of the dry weight (petroleum ether extract); Mohr and Heimann<sup>9</sup> found 15.75 per cent; Mohr and Freund,<sup>10</sup> 10.0 per cent; Polano,<sup>11</sup> 6.4 per cent; and Watanabe,<sup>4</sup> 11.26 per cent.

The average essential lipid (total lipid minus neutral fat) was 8.85 per cent of the dry weight, with total phospholipid composing 6.79 per cent, of which 2.26 per cent was cephalin, 3.55 per cent lecithin, and 0.98 per cent was sphingomyelin. Cerebrosides averaged 0.53 per cent; free cholesterol, 0.99 per cent; and cholesterol esters, 0.54 per cent of the dry weight.

The highly specialized and functionally active placental tissue is relatively high in free cholesterol and phospholipid, a characteristic of other organ tissues, in contrast to the low phospholipid and free cholesterol contents of muscle.<sup>12, 13</sup>

Thannhauser, Benotti, Walcott, and Reinstein<sup>14</sup> have reported the phospholipid analyses of normal human organs and, in general, the lipid composition of the placenta resembles that of such organs as the lung, kidney, and heart. This resemblance is especially marked in the phospholipid content and in the lecithin to cephalin ratio, which is high for the placenta.

The phospholipid to cholesterol ratio was found to be 5.2, quite similar to the ratio of 5.8 for newborn rats,<sup>15</sup> or to smooth muscle, for which Bloor<sup>16</sup> reports an average ratio of 4. In the placenta, as in newborn rats, cephalin is lower than lecithin, a relationship which is reversed as the rat matures.<sup>15</sup> Free cholesterol also is higher than cholesterol esters in young rats and placenta, whereas in older rats the latter are present in the greater amounts. The ratio of free cholesterol to cholesterol esters in the placenta, 1:0.54, is the reverse of that found by Klaus, who obtained 0.40 per cent of free cholesterol and 1.69 per cent of cholesterol esters, a ratio of 1:4.2. Bienenfeld found a ratio of 1:0.4, although her absolute values were much lower than were obtained in the present study, 0.30 per cent of free cholesterol and 0.12 per cent of cholesterol esters. Total cholesterol represented 1.31 per cent of the dry weight, while Klaus<sup>1</sup> reported 1.40, Bienenfeld,<sup>3</sup> 0.37, and Mohr and Heimann,<sup>9</sup> 1.55 per cent of the dry weight.

The guinea pig and the human being both show a lipemia in pregnancy,<sup>17, 18</sup> in contrast to many other animals, and, as Boyd has pointed out, in gross and microscopic appearance the placentas of guinea pigs and women are much alike. Boyd<sup>19</sup> has reported the neutral fat, cholesterol, and phospho-

TABLE II. AVERAGE LIPID DISTRIBUTION IN NINE HUMAN PLACENTAS

PER CENT OF TOTAL LIPID		PER CENT OF ESSENTIAL LIPID		PER CENT OF PHOSPHOLIPID	
Neutral fat	32.3	Cerebrosides	6.0	Cephalin	33.3
Essential lipid	67.7	Free cholesterol	11.2	Lecithin	52.3
		Cholesterol esters	6.1	Sphingomyelin	14.4
		Phospholipids	76.7		

\*The investigation of the composition of the placenta was a part of studies of mothers during pregnancy and lactation, the composition of their milk, and the growth of their infants. Partial support for the investigation was given by the Nutrition Foundation, Inc.





Fig. 1.—Gross specimen.



Fig. 2.—Anteroposterior views of fetus. Note that bony structure is completely normal except for absence of first cervical vertebra.

## AN UNUSUAL CASE OF HOLOACEPHALUS

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ON JANUARY 12, 1946, a 17-year-old, white primipara was admitted as a patient to the obstetric department of St. Mary's Hospital. The patient's last menstrual period had been June 18, 1945. She was having moderately strong contractions which had begun six hours before. Membranes were intact and there was no hemorrhage. Fetal heart tones, heard in the right lower quadrant, were 130, and of good quality. When the cervix had 6 centimeters dilatation, a breech presentation was definitely determined. Fetal heart tones remained 120 to 130, and of good quality. Six hours after her entry into the hospital, the patient delivered spontaneously a male child as a frank breech, in right sacroanterior position. The fetus was completely acephalic, with a large dark blood clot adherent to the neck. The color was good. The cord was pulsating, and there was no evidence of twisting or knotting. The baby's heart was beating forcibly. After approximately four or five minutes the cord was clamped, tied, and cut. The heart continued to beat for another five or six minutes; the beats became gradually weaker, and finally "death" occurred. The third stage of labor was uneventful. The cord was normal in appearance and length. Hemorrhage amounted to about 150 c.c. Vaginal examination at this time, and x-ray of the pelvis later, failed to reveal any evidence of retained or old unabsorbed bony elements.

The patient's childhood history was essentially negative. Diagnosis of pregnancy was first made four months prior to her entry into the hospital, when the patient underwent an operation for acute appendicitis. The day after this operation she noted slight, dark red, vaginal spotting, which lasted for five or six days, and then stopped completely. After the operation, she noticed transient "nagging backache" in the left lumbar region; this occurred two or three times a week and was brought on by standing for long periods. Menstrual history of the patient was essentially negative, except for rather severe dysmenorrhea the first two days of the period. Four months prior to the estimated date of the last menstrual period, the patient states she was under treatment for mild hypothyroidism and functional amenorrhea. The missed period which signalled onset of the pregnancy was mistaken by the patient as a symptom of her hypothyroidism.

Physical examination revealed no abnormalities.

The patient's husband, 19 years old, had essentially negative past history. His mother had ten children, two early abortions, and one premature child who died after two weeks of life. His sister had had three premature deliveries; two of her children are living and well, and one is a 13-year-old idiot now in an institution. The mother of the patient has two children, both living and well; she had no abortions.

*Autopsy of Fetus.*—The body was that of a 7½ months' premature male infant, born completely without a head. The body measured 30 cm. in length, and weighed 1,110 grams. External examination revealed an appendage of skin covered with hair and measuring 7 cm. in length and 2 cm. across. This appendage arose from the right side of the stump of the neck; it was soft and

## THE EFFECT OF ESSENTIAL HYPERTENSION ON PREGNANCY

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THE hypertensive pregnant patient can be classified as having either essential hypertension, malignant hypertension, arterial hypertension of known etiology, or pre-eclampsia. This paper is concerned only with essential hypertension discovered during pregnancy, its effect on the health of the mother and child, and upon the mother after termination of such a pregnancy. The pregnant patient with hypertension may ask one or more of the following questions:

1. Will pregnancy aggravate the hypertension?
2. Is the existence of hypertension a sufficient reason for terminating the pregnancy?
3. Will the hypertension influence the health of the child?

The characteristic finding in essential hypertensive disease is an elevation of the blood pressure without any signs or symptoms of renal disease. Dieckmann<sup>1</sup> defines essential hypertension in pregnancy as a state in which "a blood pressure of 140 systolic and 90 diastolic or more exists for two days or longer. This degree of pressure may be present before or during pregnancy and usually persists for six weeks or longer post partum." In this paper we have accepted Dieckmann's definition of essential hypertension as stated here. In many instances, the only sign found was an increased blood pressure. However, it was noted that the patient may have complained also of headache, unusual fatigue, dyspnea on exertion, edema, nocturia, vertigo, or tinnitus. Albumin may have been found in the urine on occasions. The absence of these additional findings suggests that the vascular tree had accommodated itself well to the elevation of blood pressure.

### Materials and Methods

In a series of 3,000 patients delivered consecutively in the Hospital of the University of Pennsylvania, there were 115 women who showed essential hypertension, as indicated by the fact that their blood pressures were 140/90 or higher on two or more prenatal visits. These patients were followed regularly throughout their pregnancies, with observations being made as to the onset of any new symptoms and the ranges of their blood pressures. The type of labor and delivery was noted in each case with particular reference to the condition of the infant at birth. A six weeks' postpartum examination was made on 90 of the 115 women.

### Observations

*First Prenatal Visit.*—The time of the first prenatal visit varied from the third to the eighth month. The majority of patients were seen for the first time during the fourth month of their pregnancies. On the first visit 60 of the 115 patients had a normal blood pressure but later developed essential hyperten-

contained no bony structure. In the upper anterior aspect of the neck stump there was a 2 cm. aperture through which opened a normal trachea and esophagus. The extremities were normally developed and presented bilateral talipes equinovarus. The back was normal; external genitals revealed testes absent from the scrotum.

*Thoracic cavity:* The pleural cavity contained nonaerated, collapsed lungs. The trachea and bronchi were normal. A moderately large thymus gland was overlying the trachea. The heart was normal in size, shape, position, etc. Myocardium and valves were normal. There was a patent ductus arteriosus and a closed foramen ovale.

*Abdominal cavity:* The liver, spleen, pancreas, gastrointestinal tract, and kidney-ureter-bladder tract were all normal in size, shape, position, etc. The adrenals were not defined, but a mass of tissue scattered retroperitoneally on the under surface of the kidney was thought to be adrenal tissue; no definite cortex or medulla was noted. The testes and associated structures were found in the abdominal cavity.

*Spinal cord:* The spinal cord was dissected out in an attempt to determine if any brain tissue was present in the cephalic end of the cord. Examination revealed normal appearing cervical enlargement and apparently normal spinal nerve roots. Grossly, there was no evidence of midbrain structure on section of the spinal cord. The meninges were intact and the cephalic end of the cord simply tapered off to the end of the closed vertebral canal at the level of the sixth cervical vertebra.

It was attempted to establish the possibility of intrauterine amputation by determining the origin and insertion of the larger neck muscles and tracing the carotid vessels. The only definite information obtained was that the trapezius muscle had normal origin and insertion, and that the three main vessels arising from the arch of the aorta were normal. Dissection of the distal portion of the internal carotid artery and jugular vein failed to reveal any definite terminus or demonstrable communication between arterial and venous systems.

*Microscopic findings:* The heart, kidney, pancreas, spleen, and spinal cord revealed no pathology. A section of the skin appendage over the anterior superior trunk revealed only ectodermal structure, no neural elements. The liver showed hemopoietic centers scattered throughout the sinusoids. The lungs showed poor delineation of alveoli. Examination of the pink-tan tissue scattered on the under surface of the kidney and posterior abdominal wall revealed embryonic adipose tissue. There was no chromaffin tissue or definitive adrenal tissue. Examination of the intra-abdominal testes revealed embryonic seminiferous tubules; no pathology was seen.

A review of the literature on acephalus shows this case to be a rare and unusual one. There is apparently no place for it in the usual classification of acephalic monsters. The cases usually reported in literature occur in twin pregnancies, the acephalic monster acting as a parasite and being kept alive by a more or less normal twin.

TABLE III. FETAL SALVAGE IN RELATION TO ESSENTIAL HYPERTENSION

	PREGNANCIES			
	NOT ASSOCIATED WITH ESSENTIAL HYPERTENSION		ASSOCIATED WITH ESSENTIAL HYPERTENSION	
	NUMBER	PER CENT	NUMBER	PER CENT
Total Conceptions	2885	100	115	100
Abortions	340	11.8	4	3.0
Premature Births	273	9.5	12	10.4
Stillbirths	56	1.2	3	2.6
Neonatal Deaths	68	2.3	1	0.8
Total	737	24.8	20	16.8

Note that the incidence of abortion, premature births, stillbirths, and neonatal deaths was less in the presence of hypertension than in its absence.

### Maternal Outcome

There were no maternal deaths among the 115 hypertensive patients before the six weeks' follow-up examination. Of 90 women who were checked at this time, one-half showed a return of the blood pressure to normal.

### Discussion

Will pregnancy aggravate a hypertension? Fifty-five of the patients exhibited an increased blood pressure on their first prenatal visit. Thirty-seven of these experienced an increase in pressure as pregnancy progressed, while the pressure of 18 remained unchanged. The fact that 60 patients entered pregnancy with a normal blood pressure and later showed an increase would lead us to believe that pregnancy does influence the hypertensive state. This increase was not permanent in all of them since the blood pressure of 50 per cent of the 90 patients followed returned to normal within six weeks of delivery, nor was it detrimental to the mother's health. There were no maternal deaths, and the only complication was an abruption of the placenta. This series is being followed so that a report may be made in 3 to 5 years after delivery. Such results might then be compared with Herrick and Tillman's<sup>2</sup> study where 15.7 per cent of maternal deaths occurred in a period of five years and eight months.

Is the existence of hypertension a sufficient reason for terminating the pregnancy? In observing hypertensive patients, one's attention is always called to the possible damage which has occurred, or is occurring, to the vascular or renal systems. Laboratory tests previously disclosed no facts of value in this connection because there was rarely enough damage to be demonstrated by such methods. Dieckmann states that the height of the blood pressure is out of proportion to the amount of edema and albumin present. Renal function is normal, and the eye grounds are normal or show a slight narrowing of the arterioles. Also, Crabtree<sup>2</sup> states that clinical findings in benign hypertension during pregnancy are essentially those of the nonpregnant state. Dexter and Weiss<sup>3</sup> noted that the amount of albuminuria gave no indication as to the course of the disease in pregnancy. It is only in severe cases of hypertension that any impaired renal function or marked eye ground changes are to be observed. The majority of patients experienced no damage to their renal and cardiac systems from repeated pregnancies. Two patients were known to have impaired kidney function; several showed some early retinal changes; the remainder revealed

sion, while 55 women exhibited hypertension on their first visit. Of this latter group, 38 had had one or more previous pregnancies; the remaining 17 were pregnant for the first time.

Table I summarizes the range of the blood pressure of these two groups on their first prenatal visits.

TABLE I. RANGES OF BLOOD PRESSURES ON THE FIRST PRENATAL VISIT

BLOOD PRESSURE	PAROUS	NULLIPAROUS	TOTAL
Under 140/90	41	19	60
140-149	13	9	22
150-159	10	3	13
160-169	8	2	10
170-179	2	1	3
180-189	0	0	0
190-199	3	1	4
200 - over	2	1	3
Total	38	17	55

TABLE II. AGE DISTRIBUTION OF THE 115 PAROUS AND NULLIPAROUS PATIENTS

AGE	PAROUS	NULLIPAROUS
15 - 19	0	2
20 - 29	16	22
30 - 39	59	12
40 - 49	4	0
Total	79	36

The majority of instances of hypertension in the parous group occurred between the ages of 30 and 39, while in the nulliparous group the greater number was between 20 and 29 years of age.

Of the 79 parous patients, 43 had hypertension prior to the present pregnancy, 14 were normal on their first prenatal visit, and 18 had no previous record. Four patients had suffered from previous pre-eclampsia with a resultant increase in blood pressure early in this pregnancy but with no recurrence of pre-eclampsia or eclampsia.

### Prenatal Course

During the prenatal course, 52 of the 115 patients experienced albuminuria of varying degrees, the majority exhibiting only a trace. The remaining 63 were free of albumin. Two women showed impaired renal function as pregnancy progressed; six had only slight involvement, as shown by lowered urea clearance tests. The symptoms of headache, vomiting, and edema occurred with the same frequency as in normal pregnancy. The eye grounds of 33 patients were examined. Twenty-one were found to have early sclerotic changes with some spasm, two showed marked arteriosclerosis, and ten were normal. One patient had an abruption of the placenta in the eighth month of pregnancy.

Eight patients experienced blood pressures of at least 200/100 at some time during their pregnancies. Four of these individuals had their pregnancies interrupted either by therapeutic abortion or hysterotomy. The remaining four delivered normal infants at term. Eleven patients had blood pressures between 190/100 and 200/100. Nine delivered normal infants, one aborted, and one delivered a stillborn child.

### Influence of Hypertension on Fetal Mortality

Of 2,885 pregnancies not associated with essential hypertension, 737 (25 per cent) ended in either abortion, premature birth, stillbirth, or neonatal death. Of 115 pregnancies in patients with essential hypertension, 20 (17 per cent) ended in this manner. Table III shows these distributions.

that there is little danger of any maternal accident. A permanent increase did occur in the hypertensive state in 45 of the 115 patients. This increase did not appear significant and seemed in accord with the rise that would occur naturally as the course of the disease.

### Conclusions

1. Pregnancy aggravates the hypertensive state both in parous and nulliparous individuals.
2. The existence of hypertension itself is not sufficient reason for terminating the pregnancy.
3. The fetal death rate is not increased in the presence of essential hypertension.

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no abnormalities in either their renal or cardiac systems or in their eye grounds. Our laboratory studies agreed with the findings of Dieckmann, Crabtree, and Dexter and Weiss. Therefore, the clinician must treat these patients according to the signs and symptoms they present, rather than wait for positive findings from the laboratory.

Marked increases in blood pressure were seen in 2 patients in this group. One patient, whose initial blood pressure was 140/80, reached 240/130 at term. The other woman started pregnancy with a blood pressure of 150/100, which ultimately reached 200/130. Both these patients came through their labors well and delivered normal full-term infants. In addition to these, six women in our series had blood pressures over 200/100. Four of these patients had their pregnancies interrupted, while two delivered normal infants at term. We believe, therefore, that pregnancy will aggravate an existing hypertension, but usually does so with no demonstrable injury to the mother's health.

We do not feel that there is enough significant damage to the patient's cardiac or renal systems to warrant interrupting a pregnancy merely because of the elevation of blood pressure or because of the appearance of a small amount of albumin. There being no maternal deaths in this series and only one case of abrupted placenta, it would seem that such accidents rarely accompanied the hypertensive state. If, however, one does find marked eye ground changes or impaired cardiac or renal function, the possibility of interrupting that pregnancy should be considered.

Will the hypertension influence the child? Dexter and Weiss<sup>5</sup> studied 20 infants of hypertensive mothers. Five were premature and two were stillborn. They, therefore, advised the interrupting of pregnancy as near as possible to the thirty-second week in order to reduce the incidence of stillbirths. Dieckmann<sup>3</sup> states that in his series of pregnancies 21 per cent of infants died. In Browne and Dodds' series<sup>6</sup> of 239 pregnancies, 36.5 per cent of infants failed to survive. We have not found that maternal hypertension influences the infant to such a degree. The incidence of abortions, premature deliveries, and stillbirths in our hypertensive patients was not significantly increased. Our fetal death rate was 17 per cent; while Dieckmann and Browne and Dodds had 21 and 36.5 per cent, respectively.

### Summary

It is our belief, therefore, that the presence of a high blood pressure in a pregnant patient who shows normal laboratory findings, but who may have some albuminuria, edema, or headaches, should not contraindicate the carrying of such a pregnancy to term. A few additional precautions, such as bed rest, control of the patient's weight, and sedation, are helpful. Any marked increase in the severity of the symptoms should be investigated for the possibility of an acute progression of the disease, although in our experience this has been negligible. The patient should be informed that the possibility of fetal complications is no greater than in the absence of hypertension. Persons who are desirous of having one or two children should be told that, with adequate prenatal care, the possibilities of delivering a normal healthy infant are good and



### Case Report

Mrs. A. W., a 55-year-old white housewife, gave the following history: In 1942 she began to experience climacteric symptoms in the form of hot flashes, nervousness, and irregular menstrual periods. In May, 1944, at the age of 54 years, the menses ceased altogether. In February, 1945, at the age of 55 years, after a period of amenorrhea of nine months' duration, she noted onset of intermittent vaginal bleeding and soreness of the breasts for a period of two weeks. She also became aware of a swelling in her abdomen which was notably tender, and she thought that she might be pregnant.

In March, 1945, while lying on her abdomen and reaching for a toy under the sofa, she had a sudden excruciating pain in the right upper quadrant and in the right shoulder, accompanied by abdominal swelling. The pain lasted throughout the day and was relieved only by a narcotic. After five days the abdominal pain and swelling subsided. She was informed by her physician that she had a pelvic tumor and was referred to the gynecologist for diagnosis and treatment.

Her complaints at the time of consultation were tiredness, nervousness, and slight abdominal pain. During the following month there was a recurrence of the bleeding, profuse enough to require two or three sanitary napkins daily. She experienced the same sensations as those which accompanied her previous normal menstrual periods.

Her family history was irrelevant. She had the childhood diseases of measles, mumps, and scarlet fever. Her menarche began at the age of 14 years. The menstrual periods were normal and regular until the appearance of the menopausal syndrome. She was operated upon at the age of 17 years, when the appendix and a right ovarian tumor were removed. The nature of this tumor could not be ascertained. Her obstetric history revealed that she was a gravida iii, para ii, with one miscarriage at four and one-half months.

The physical examination revealed a small, slender woman of about the stated age and weighing 100 pounds. The temperature, pulse, and respirations were normal. The blood pressure was 108/80. The circulatory, respiratory, and alimentary systems showed no significant changes. The pelvic examination revealed a clean lacerated cervix. The uterus was situated anteriorly, was freely movable, regular in contour, and normal in size and consistency. The right adnexus was uninvolved. The left adnexus contained a cystic, semisolid mass about the size of an orange. Upon the strength of the history and physical findings, a diagnosis was made of a left ovarian tumor, probably of the granulosa-cell type.

An operation was performed on April 24, 1945, under cyclopropane and ether anesthesia. The abdominal cavity was found to contain approximately two liters of serosanguineous fluid. The origin of this fluid was apparently a large collapsed cyst which was attached to a multilocular mass in the left adnexus. The uterus and left tuboovarian mass were removed (the right ovary had been removed at the age of 17 years).

The postoperative course was characterized by a daily elevation of the temperature to 100° F. for four days. The remainder of her convalescence was uneventful. She was discharged on the twelfth postoperative day in a satisfactory condition.

The laboratory data revealed a hemoglobin of 11.3 Gm. red cell count of 4,330,000, and a white cell count of 7,000. The polymorphonuclear neutrophils were 67 per cent; lymphocytes, 30 per cent; monocytes, 2 per cent; and eosinophiles, 1 per cent. The coagulation time was four minutes, while the bleeding time equaled two and one-fourth minutes. The sedimentation rate was 16 mm. in one hour. Serologic tests for syphilis were negative. The urine contained nothing of significance.

## GRANULOSA-CELL TUMOR OF THE OVARY\*

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**G**RANULOSA-CELL tumors of the ovary have been thoroughly studied recently by several investigators (Dockerty,<sup>3</sup> Bland<sup>2</sup>). Much of the work has dealt with a review of old pathologic material to which have been added new cases. The literature reveals but a few instances where the diagnosis of this tumor was made preoperatively. The following case seemed worthy of addition to the growing list of these interesting tumors, not only because of their relative rarity (1.63 per cent of ovarian tumors as found by Hodgson, et al.<sup>7</sup>), but because of the clinical history which led to the correct clinical diagnosis before operation.

Although granulosa-cell tumors were described almost a hundred years ago,<sup>10</sup> over one-half of approximately 500 cases have been recorded in the literature in the past decade. Robert Meyer,<sup>8</sup> must be given the credit for the awakening of interest in this gynecologic entity which has received more attention during the past five years than any other ovarian tumor. As to the histogenesis as promulgated by Meyer, these tumors presumably arise from granulosa-cell rests in the hilus of the ovary. This is now at variance with views held by recent observers. Furth and Butterworth<sup>6</sup> have produced granulosa-cell tumors in mice by the use of the x-ray. Biskind and Biskind<sup>1</sup> feel that the pituitary plays a part in the process.

Clinically, over 50 per cent of these tumors occur during the childbearing period;<sup>3</sup> 5 to 10 per cent, before the age of puberty; the rest, after the menopause. In children, the symptoms are mainly those of precocious menstruation and somatic development. Amenorrhea, menorrhagia, or metrorrhagia may be encountered during the childbearing period. After the menopause, the most common symptom is cyclic bleeding. Enlarged and painful breasts also may be encountered. According to Dockerty,<sup>3, 4</sup> amenorrhea ascribed to the menopause may be the first symptom of a granulosa-cell tumor. Assays of blood and tumor tissue in humans and in animals with experimentally produced tumors have shown large amounts of estrin to be present.<sup>2, 3</sup> The symptoms produced by these tumors are referable to the increase in this hormone.

Pathologically, the tumor shows considerable variation in its gross and microscopic appearance. It may be only a few millimeters in size or it may be large enough to occupy most of the abdominal cavity. The surface is usually smooth, and, like most ovarian tumors, it is oval or round. The cut surface reveals a solid tumor, but it may become cystic as it enlarges. It is often associated with cysts of the ovary. Its color is distinctly yellow, which helps to distinguish the tumor from other ovarian neoplasms.

The histologic structure of a granulosa-cell tumor is also quite varied. The tumor cells may be arranged into many patterns, giving rise to the many descriptive terms, such as *folliculoid*, *cylindromatous*, *pseudo-adenomatous*, and *parenchymatous*.<sup>9</sup> In some tumors the cells are irregular, pleomorphic, and anaplastic, and may well be mistaken for a sarcoma. On the other hand, many are well differentiated and are relatively benign. The tumor is essentially a carcinoma with all its inherent gradations of malignant possibilities. In about 10 per cent of the cases the tumor is bilateral.<sup>5</sup> It spreads by local extension and metastases in the liver, pleura, and meninges.

\*Dr. M. B. Dockerty of the Mayo Clinic gave valuable assistance and advice in the preparation of this paper.

Sections of the endocervix showed relatively few glands. Some were mainly of the simple variety. There was some variation in their size, and some had a cystic dilatation. A few had a tendency to coil. The glands were lined with columnar epithelium. The majority of the nuclei were basal in location, and a fair number were in mitosis. The cells of the interglandular stroma were closely packed at the base, but were loosely arranged near the surface. Mitotic figures also were encountered here. The blood supply appeared adequate. Many of the capillaries were distended with blood. The endometrial picture was compatible with that described by others in connection with granulosa-cell tumors.

The myometrium presented no distinctive features. Connective tissue increase was not apparent. The blood vessels showed no definite changes.

**Diagnosis.**—Granulosa-cell tumor of the ovary (cylindromatous type); hyperplasia of the endometrium; cystic cervicitis.

Figs. 1 and 2 show a typical pattern of the tumor at various magnifications.

### Discussion

The symptom of amenorrhea may have been the first sign of the presence of a granulosa-cell tumor. The episodes of uterine bleeding have been explained on the basis of a "withdrawal" phenomenon of estrogen level in the blood circulation due to changes in the tumor.

The rupture of the cystic tumor is not a common occurrence. In a different type of ovarian malignancy, such a rupture would invariably disseminate the growth throughout the abdominal cavity. The pain, with its distribution, no doubt, was due to peritoneal and diaphragmatic irritation.

Associated pathologic changes are usually present with a granulosa-cell tumor. As in this case, cystic endometrial hyperplasia is to be expected. Fibromyoma, adenomyoma, and general uterine hypertrophy are commonly found. Carcinoma of the endometrium and endocervix, as well as hyperplasia, fibroadenoma, or carcinoma of the breasts may be encountered also.

The management of a granulosa-cell tumor calls for conservatism in the young patient and radical treatment in the old, as was followed in this case. This patient was alive and well one year after the removal of the tumor. Periodic examinations for detection of possible recurrences should be practiced, particularly where there is a history of rupture.

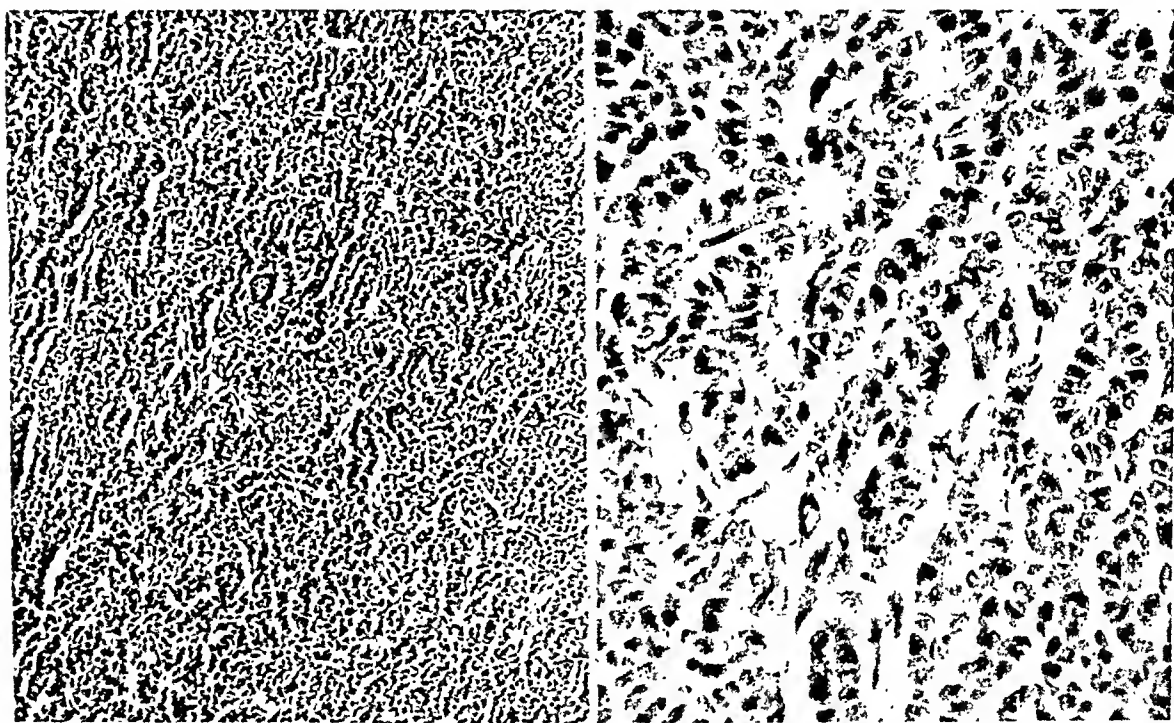
### Summary

A case of granulosa-cell tumor of the cylindromatous type has been reported. The patient, a 55-year-old woman, had clinical symptoms and physical findings sufficiently characteristic to suggest the diagnosis preoperatively. A brief consideration of the incidence, histogenesis, and pathology has been presented.

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*Pathologic report.*—Specimen consisted of a totally resected uterus and a collapsed cystic tumor of ovarian origin. The uterus measured 8 cm. in length and 6.5 cm. in diameter across the fundus. It weighed 93 Gm. The cervix had been previously sutured. The cervical canal showed no special changes other than a few small retention cysts. The myometrium was of normal appearance and measured 1.8 cm. in thickness. The tumor had been previously sectioned and consisted of a collapsed amorphous cyst showing considerable distortion. A Fallopian tube on its surface could not be demonstrated. On sectioning, the tumor was composed of a cystic portion which, on reconstruction, measured approximately 9 cm. in diameter. Its lining was smooth and somewhat wrinkled. A small daughter cyst was filled with blood. The other half of the tumor was solid, and was composed of moist, structureless tissue having an intensely yellow color. Its consistency was rather soft. A few small hemorrhagic areas were scattered within the mass. The tumor was surrounded by a narrow shell of what appeared to be normal ovarian tissue.



Figs. 1 and 2.—Photomicrographs (X150 and X530, respectively) stained with hematoxylin and eosin; and showing the typical cellular arrangement of the granulosa-cell tumor removed from the patient.

Microscopic examination of the sections stained with hematoxylin and eosin and taken from the solid portion of the tumor, revealed a solid pattern of hyperchromatic cells arranged mainly in rows supported by fine strands of connective tissue and capillaries. This basic pattern was cylindromatous, and it was partly disrupted by the formation of clusters of cells surrounding small cystic spaces. The latter appeared to be produced by liquefaction and resembled somewhat the so-called Call-Exner bodies, rather than the rosette arrangement of cells surrounding a lumen. Under higher magnification, the cells appeared to be of the granulosa type. Their nuclei were hyperchromatic and stained uniformly. The nucleoli were visible, but were not outstanding. Mitotic figures were extremely scarce. Where the cells were not so crowded, a definite rim of eosinophilic cytoplasm could be seen. Sections from the wall of the larger cyst showed a thick fibrous wall lined by a wide zone of granulosa cells having a pattern similar to that of the solid portions of the tumor.

In reviewing the records of the Mayo Clinic we have found five cases in which lipomas have been removed surgically from the broad ligaments. Two of these we wish to report in detail.

### Report of Cases

CASE 1.—The patient was a 36-year-old white woman admitted Sept. 17, 1935, with a mass in the right perineal region the size of a large grapefruit. This mass had been enlarging for four years. It could be palpated as it bulged into the right side of the vagina and rectum and as it extended into the right labia and right buttock. The mass was reducible but recurred with coughing or straining. It had caused the patient intermittent hesitancy of urination. Because of its consistency and location this mass was thought to be a perineal tumor which had arisen in the right broad ligament.

The patient had always been in good health, except for an attack of influenza in 1918. Both parents and three brothers were alive and gave a history of good health. She had undergone three normal pregnancies and deliveries. Her menstrual periods were regular, occurring approximately every twenty-eight days and persisting for three or four days. Examination of urine for albumin, sugar, bacteria, and microscopic cellular elements gave negative results. The concentration of hemoglobin was 14.9 Gm. per 100 c.c. of blood. There were 8,300 leucocytes per cubic millimeter of blood. A roentgenogram of the thorax was negative and a Kahn test gave negative results. The blood pressure was 128/84. The temperature was 99.4° F., and the pulse 86. The patient was 65 inches (165 cm.) tall and weighed 100 pounds (45.4 kg.). The remainder of her physical examination did not reveal any abnormalities.

On Sept. 20, 1935, while the patient was under nitrous oxide, oxygen, ether, and ethylene anesthesia, a low midline incision was made. A large fibromyxolipoma presented in the right broad ligament and extended along the right side of the vaginal canal to present in the perineum anterior and to the right of the vagina. An incision was made on the posterior surface of the right broad ligament and the tumor was removed. Subtotal abdominal hysterectomy, bilateral salpingectomy, and left oophorectomy were carried out. The right ureter was freed and brought anterior to the cervical stump, which was then used to block the opening through which the tumor had descended. The appendix showed evidence of previous inflammation and was removed. The incision was closed with one row of single continuous chromic catgut No. 1 in the peritoneum and a row of double continuous chromic catgut No. 1 in the fascia. The pathologist reported the tumor to be a fibromyxolipoma weighing 500 Gm. Chronic metritis and bilateral chronic salpingitis were present. When the patient was dismissed to go home on the twenty-first postoperative day she was in good general condition and the incision was well healed.

The patient returned July 8, 1936, with a recurrence of a mass of almost the identical size located at the previous site. This was removed through a perineal incision while she was under cyclopropane, oxygen, and carbon dioxide anesthesia and in a lithotomy position. The tumor was firmly adherent to all the surrounding structures, to the base of the bladder, and to the right side of the vagina. Oozing of blood was difficult to control, and a large iodoform pack was required to control it. The pathologist reported the tumor to be a fibromyxolipoma weighing 500 Gm. The pack was removed on the sixth postoperative day. When the patient was dismissed to go home on the seventeenth postoperative day, the incision was well healed.

The patient again returned Aug. 7, 1941, stating that a recurrence of the perineal mass had been slowly developing for two years, and that enlargement had been rapid in the preceding six months. On Aug. 9, 1941, while she was

## LIPOMAS OF THE BROAD LIGAMENT EXTENDING BEYOND THE CONFINES OF THE PELVIS

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A RETROPERITONEAL lipoma is an uncommon finding; moreover, the occurrence of a lipoma in the broad ligament is even more unusual. Lipomas of the broad ligaments are of interest because of the gynecologic diagnostic problem that they may present, the difficulty that surgical extirpation may pose and the problem that is raised by an occasional recurrence. Our interest was aroused in these tumors after we had had occasion to remove lipomas arising in the broad ligament in two patients. In one patient the lipoma presented in the perineum and in the other the lipoma presented in the medial aspect of the buttock, making an exit from the pelvis through the right obturator foramen.

In 1932, Bettman and Serby<sup>1</sup> reviewed 307 cases of retroperitoneal tumors found in the literature, the majority of which were proved lipomas or liposarcomas. In 1942, Neale<sup>5</sup> reviewed the cases in which retroperitoneal tumors had been removed surgically at the Mayo Clinic prior to that time. He found 22 of the tumors to have been lipomas, and an additional 32 to have been liposarcomas. A follow-up of the 22 patients who had had lipomas revealed that five had died in the immediate postoperative period, eight had died of subsequent recurrence, one had died of myocardial failure, and eight were alive and well. A follow-up of the 32 patients who had had liposarcomas revealed all to have died. Four died immediately after operation, and the remainder died ten months to ten years after operation; only two patients lived more than four years. All deaths were attributed to recurrence of the tumor. The retroperitoneal lipomas reported in this study had usually enlarged to a considerable size before the patient or the physician discovered the presence of the tumor mass. The high surgical mortality rate is to be attributed to the largeness of the tumors as well as to the vigorous bleeding encountered when they were dissected free from the attachments to the mesentery of the large and small bowel, as well as to the large blood vessels.

In 1939, Stagg and Hunter<sup>8</sup> reviewed the cases of lipomas of the broad ligament that had been reported in the literature. They reported two cases and found 14 others, two of which Lockyer<sup>4</sup> regarded not as true neoplasms, but rather as fatty material that had spilled from a dermoid cyst. This would make a net total of 14 cases of true lipomas of the broad ligament that have been reported. Cases have been reported by Pollock<sup>6</sup> in 1852, Klein<sup>3</sup> in 1909, Lockyer in 1919, Rawls<sup>7</sup> in 1926, and Kantner<sup>2</sup> in 1935. We have been unable to find additional reports of cases following those of Stagg and Hunter. Probably other cases have occurred but have not been reported in the literature because it was considered that these tumors are benign. In the cases reported, lipomas occurred in the right broad ligament in four, in the left broad ligament in three, they were bilateral in three, and the site was not reported in four. Preoperatively, the majority had been thought to be ovarian cysts. In no case did the lipoma extend beyond the confines of the pelvis.

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mass about  $1\frac{1}{2}$  inches (3.8 cm.) lateral to the anus. A plane of cleavage was found, and a lipoma the size of a large grapefruit was shelled out. Hemostasis was secured and the incision was closed with interrupted catgut sutures in such a manner as to obliterate the space that had been occupied by the lipoma. The incision was closed without drainage and healed by first intention. The pathologist reported the tumor to be a lipoma showing many regions of inflammation and fibrosis. Postoperatively, the patient was placed on a residue-free diet for seven days. The diabetes was controlled with small amounts of protamine zinc insulin and regular insulin for fourteen days, after which she did not require further insulin. When she was dismissed to her home on the nineteenth post-operative day she was in good general condition and both incisions were well healed. A recent communication from her attending physician states that there has been no evidence of recurrence of the lipoma.

The remaining three cases observed were as follows:

In the third case a lipoma measuring 3 by 2 by 1 cm. was removed from the right round ligament of a 32-year-old white woman in the course of subtotal abdominal hysterectomy which was being done for severe menorrhagia.

In the fourth case a small lipoma was removed from the right broad ligament of a 45-year-old white woman in the course of total abdominal hysterectomy for severe menometrorrhagia.

In the fifth case a lipoma having a diameter of 9 mm. was removed from the left round ligament of a 50-year-old white woman in the course of total abdominal hysterectomy for adenocarcinoma of the fundus of the uterus.

### Comment

One cannot fail to be impressed by the fact that local recurrence of retroperitoneal lipomas, considered to be benign by the microscopist, is rather common and that in a number of such cases the termination is fatal. There is another reason to view these fatty retroperitoneal tumors with concern, for a high percentage will show sarcomatous tissue present. However, it would appear that lipomas that occur in the broad ligament are, as a rule, of a more benign nature than lipomas in other sites.

Lipomas of the broad ligament are usually diagnosed preoperatively as ovarian tumors. However, in the two cases that we reported, one had to distinguish the lipoma from an obturator hernia, which was made possible by noting the consistency of the mass and the fact that it moved as a distinct unit whenever it was reduced. In deciding on the proper surgical approach for removing such lipomas, one can attempt removal through the approach where the maximal mass of tissue presents; that is, through the abdomen or through the posterior approach. Even then one may find it necessary to change to the alternate approach in order to effect a removal of the tumor.

A site for potential herniation was provided by the removal of the lipomas in the two cases that we have reported. In one instance an attempt was made to prevent herniation by suturing the cervical stump over the defect. Subsequently, following a recurrence of the fibromyxolipoma a true hernia did develop, and this was repaired through an abdominal approach by removing the sac and obliterating the tissue space by purse-string sutures. In the second case, an attempt was made to close the space which the lipoma occupied by approximating the tissues with interrupted catgut sutures.

under nitrous oxide, oxygen, and ether anesthesia, a secondary low midline incision was made. A true hernia with an opening through which the fist could pass was found on the right side of the pelvis behind the cervical stump. This opening led to the perineum. There was no recurrence of the fibromyxolipoma. The hernial sac was inverted and excised and the cavity was obliterated by a running purse-string suture. It was thought advisable to remove the cervical stump and right ovary. The sigmoid was used to cover the unperitonized surface on the right side of the pelvis. The pathologist reported chronic cystic cervicitis with cervical erosion and chronic cystic oophoritis of the right ovary. When the patient was dismissed to go home on the twenty-fourth postoperative day, she was in good general condition and the incision was well healed. She was re-examined by us on Sept. 6, 1944, and was found to be without evidence of recurrence of the lipoma or hernia. There was a slight cystocele, but this was not surgical.

CASE 2.—The patient was a 37-year-old white woman admitted July 5, 1945, with a mass 5 inches (13 cm.) in diameter that was presenting midway between the anus and the right ischial tuberosity. This mass had been enlarging for one year. The mass could be palpated as it glided along the vaginal canal. It could be reduced but it recurred with coughing or straining. Sitting for any length of time brought on pain that extended down the back of the right leg and up into the lower lumbar region. The consistency of the tumor was such that it was thought to be a lipoma arising in the broad ligament and leaving the pelvis through the right obturator foramen.

The patient had had a history of rheumatic fever during childhood and had had a peritonsillar abscess on two or three occasions. She had undergone three normal pregnancies and deliveries. Her menstrual periods were regular, occurring approximately every twenty-eight days and persisting about seven days. She had known for three years that she had diabetes mellitus and had controlled it by eliminating starches from her diet. She tested her urine every other day: the tests usually did not show glycosuria. Her mother had died of dropsy at the age of 56 years and her father had died of cardiac disease at the age of 55 years. The patient was 65 inches (165 cm.) tall and weighed 190 pounds (86.2 kg.). The blood pressure was 145 mm. of mercury systolic and 90 diastolic. The temperature was 98.4° F., and the pulse 90. Her physical examinations did not reveal any other abnormalities. Urinalysis revealed a specific gravity of 1.030, acid reaction and albumin grade 2 on a basis of 1 to 4, in which 1 designates the mildest and 4 the most severe condition. Benedict's test for sugar gave slightly positive results and 6 cells per high-power field were observed. The concentration of hemoglobin was 14.0 Gm. per 100 c.c. of blood; erythrocytes numbered 5,330,000, and leucocytes 11,400 per cubic millimeter of blood. The Kahn test gave negative results. A roentgenogram of the thorax was negative. The fasting blood sugar was reported to be 208 mg. per 100 c.c.

On July 14, 1945, with the patient under nitrous oxide, oxygen, and ether anesthesia a primary low midline incision was made with excision of the umbilicus. A lipoma originated in the right broad ligament, extended down the right side of the vagina and made its exit from the pelvis through the right obturator foramen. An attempt was made to remove the tumor from above but some bleeding was encountered and it was thought advisable to close the abdominal incision by bringing the full thickness of peritoneum, muscle, and fascia on the left of the abdomen beneath the full thickness of the right side for 1 inch (2.5 cm.), using a single continuous chromic catgut No. 1 in the first row and double continuous chromic catgut No. 1 in the outer row. The patient was then placed in lithotomy position and a vertical incision was made over the lipomatous



# ADULT MEDITERRANEAN ANEMIA COMPLICATED BY PREGNANCY

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**M**EDITERRANEAN anemia (Cooley's) has long been recognized<sup>1</sup> as a highly fatal disease of childhood. It is characterized by chronic progressive anemia, splenomegaly, reticulocytosis, resistance of red corpuscles to hemolysis by hypotonic saline solutions, lack of response to any therapy, and its familial and racial incidence. The red corpuscles vary greatly in size, contain little pigment, often show basophilic stippling, primitive forms, and target cells. A similar but less severe type of anemia occurring in adults has recently been recognized,<sup>2-4</sup> and a number of cases reported. Some of these cases include more than one generation and reveal a high familial incidence.<sup>5</sup> The case reported here is the only one we know of with the diagnosis being made while the patient was pregnant, and observed during the course of and subsequent to the pregnancy.

The purpose of reporting this case is to direct the attention of obstetricians to the possibility of Mediterranean anemia as a cause of unexplained anemia in the pregnant female and to show the management of such a case which we have followed.

## Case Report

**CASE 5464.**—Mrs. M. D., a 27-year-old Italian-French, married, former Army nurse reported to the Obstetrical Clinic on Nov. 10, 1944.

**Family History.**—The patient's father was born in Italy, was 53 years of age, and was living and well. Her mother was born in France, and died at the age of 35 years from an unknown cause which had produced high blood pressure and paralysis. The patient had four siblings, three of which were living and well. The fourth had a history of mild anemia and sallow complexion.<sup>6</sup>

**Past History.**—The patient was born in California, and had had diphtheria in childhood. Sallow color of the skin had been present since childhood. At the age of 12 years noted dyspnea was present, with parietal pressure and a throbbing pain during the day, aggravated by exercise, and becoming constant over a two-year period. Anemia was noted on examination at the age of 15 years, and again at the age of 19 years. Hyperthyroidism (basal metabolism rate +40 to +50) at the age of 16 years was controlled with Lugol's solution and bromides until the age of 19 years, when a thyroidectomy was performed. Anemia during this interval was treated with ferrous sulfate. The patient was told her hemoglobin was low but that the red corpuscles were normal. No history of malaria or jaundice was elicited. The patient had entered and completed nurses' training and entered the Army Nurse Corps. She had coccioidomycosis at Williams Field, Arizona, in September, 1943, with a normal convalescence. Menses: onset at the age of 12 years, periods occurred every 28 days for five days without dysmenorrhea. (Gravida i (present)).

**Present Illness.**—Anemia was present, which was diagnosed at the age of 15 years, as noted above. The patient had been repeatedly examined for anemia and treated with iron, anti-PA liver extract, and diet for many years, never attaining a normal blood picture. No paresthesias, tongue sore-

If a patient has a reducible mass in or near the perineal region, the physician must consider the possibility of its being a lipoma. If this mass can be felt to enter the pelvis, gliding alongside of the vaginal canal, he must consider the possibility of its being a lipoma of the broad ligament extending beyond the confines of the pelvis or an obturator hernia.

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weakness and fatigue and laboratory findings of icterus index 16, indirect Van den Bergh 3.53 mg. per cent and urobilinogen 4+. White blood cells were normal throughout, varying from 7,000 to 12,000. There were no abnormal-

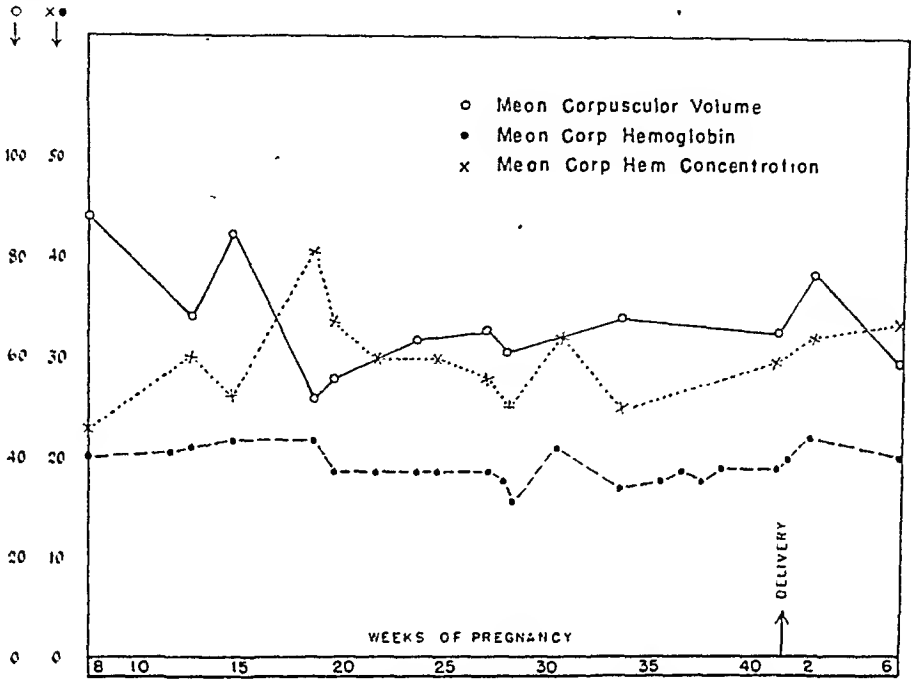


Fig. 2.

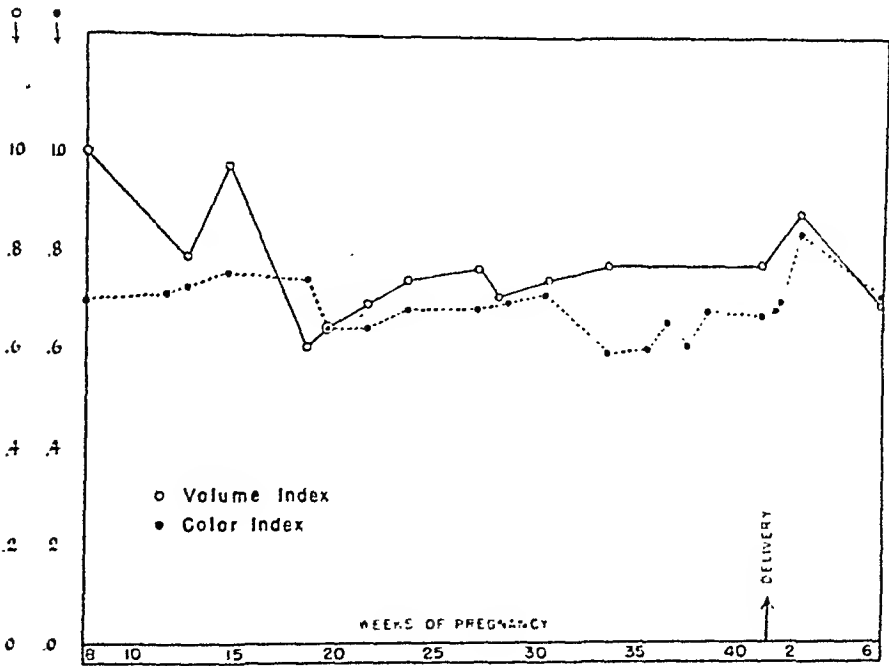


Fig. 3.

ities noted in the leucocytes or in the differential counts on repeated blood smears. But the smears showed many abnormalities of the red corpuscles, including basophilic stippling, target cells, oval cells, poikilocytosis, polychromasia, and anisocytosis. An occasional nucleated red cell was present.

ness, excessive menses, hematuria, tarry stools, or diarrhea to account for anemia. Last menses occurred Sept. 23, 1944. Slight nausea and vomiting of pregnancy noted.

*Physical Examination.*—A well-developed and well-nourished young woman with a sallow complexion. Head and neck: mucous membranes pale; tongue papillae normal; thyroidectomy scar present. Heart and lungs: soft apical systolic murmur transmitted to left axilla and precordium; heart size normal by x-ray. Blood pressure: 120/80. Abdomen: Spleen not felt; liver palpable at right costal margin. Extremities: Nails thin and brittle. Neuro-muscular and lymphoid system: Normal. Pelvic: Uterus size of six to eight weeks' pregnancy. Pelvic measurements: Adequate; large gynecoid pelvis shown by Caldwell-Moloy pelviography.

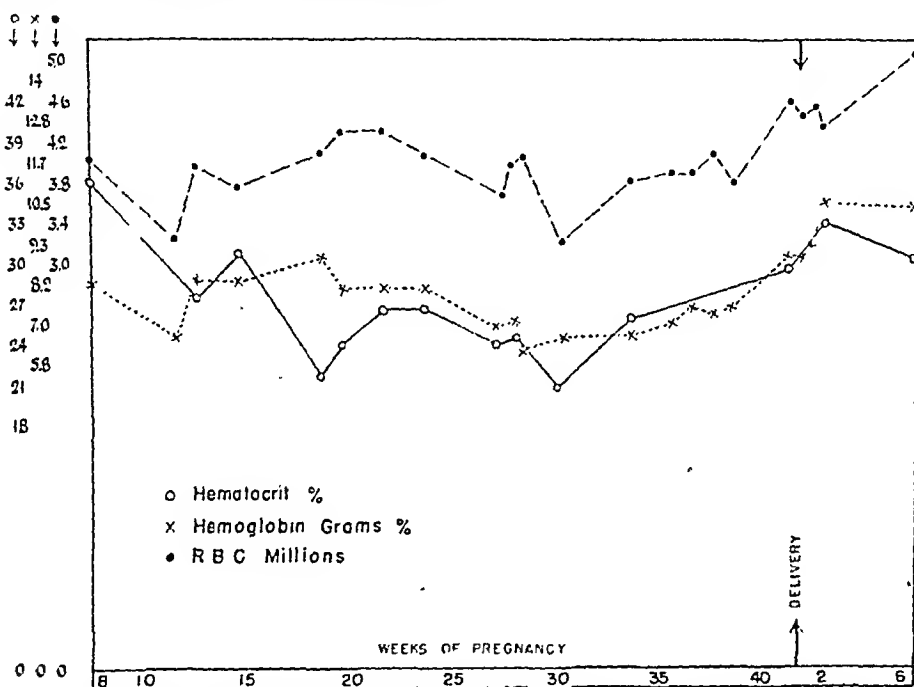


Fig. 1.

*Laboratory Investigation and Course.*—Obstetrical: the patient progressed normally except for a weight gain from 143 pounds on her initial visit to 187 pounds one week before delivery. Eleven pounds was gained during the last month in spite of rest, salt-free diet, and limitation of fluids. She was hospitalized during the last week with a loss of 8 pounds in weight before going into labor on July 7, 1945. Labor, while not prolonged, was severe. She was delivered by outlet forceps of a 9 pound, 2 ounce female. Postpartum course was uneventful except for a transfusion reaction following delivery consisting of chills and fever. The transfusion was given as a prophylactic measure with cross-matched whole citrated blood. The cause of the reaction was unknown. One week later the spleen was palpable at the left costal margin for the only time during our period of observation, and there was an icteric tinge to the sclera.

*Blood Picture.*—Blood determinations were taken throughout pregnancy and for one month following delivery (Table I). Kahn: negative. The curves of these determinations are shown in the three charts (Figs. 1, 2, and 3). Reticulocytes were elevated on twelve determinations between 2 per cent and 5.3 per cent, the highest number appearing following an episode of red-blood cell hemolysis on March 26, 1945, as evidenced by symptoms of increased

Blood count of infant at six weeks: Red blood cells, 3.87 million; hemoglobin, 13 Gm.; white blood cells, 12,400; polymorphonuclears, 37; lymphocytes, 54; mononuclears, 5; eosins, 4. There was an occasional target cell present.

We were able to obtain blood studies of the one sister mentioned above who was also an Army nurse. They were as follows: red blood cells, 5.02 million; hemoglobin, 11.2 Gm.; white blood cells, 7,200; polymorphonuclears, 72; juvenile, 1; lymphocytes, 24; monocytes, 3; platelets, 225,000; ieterus index, 7.2; mean corpuseular hemoglobin, 22.3; mean corpuseular hemoglobin concentration, 35; color index, 77; red cell fragility is given in Table III.

TABLE III. RED CELL FRAGILITY TEST ON SISTER

	SISTER	CONTROL
Initial hemolysis	0.38%	0.42%
Complete hemolysis	0.28%	0.36%

*Treatment.*—Ferrous sulfate up to 4 Gm. daily was started empirically while we were attempting to diagnose the anemia. When it was shown to be of no value in alleviating the anemia, liver extract, using 55 anti-PA units per week for two weeks, followed by 22 units per week for four weeks, was given. This produced no marked reticuloocyte response nor rise in either red cells or hemoglobin. Following the first gastric analysis which showed no free HCl and a low total acidity, we gave 90 drops of dilute HCl three times a day. The patient said she noted a relief of the "bloating" she had experienced for a number of years and was enthusiastic about continuing the HCl even after delivery. This may have been psychic but it was the only treatment given which subjectively or objectively benefited the patient. As a matter of fact, she thought our procedure of taking numerous blood samples was hardly the proper treatment for anemia, and she no doubt had a good point. Vitamin B complex and dicaleium phosphate with viosterol were also given.

### Comment

For the greater part of pregnancy the values for the hemoglobin and hematocrit readings are low, while the red cells are diminished to a lesser degree. Consequently all the calculations derived from these determinations (mean corpuseular volume, mean corpuseular hemoglobin, mean corpuseular hemoglobin concentration, volume index, and color index) are low. The curve of the color index, being the mean corpuseular hemoglobin times a factor is identical with the curve of the mean corpuseular hemoglobin. For the same reason the curve of the volume index is the same as the curve of the mean corpuseular volume. There is no constant relation between hematocrit and hemoglobin or between the hematocrit and red cells, except that all three determinations rose during the last week of pregnancy.

The diagnosis of adult type of Mediterranean anemia has been made on the basis of a chronic hemolytic hypochromic microcytic type of anemia not responding to iron, Vitamin B, or anti-PA treatment; red-cell fragility tests, showing increased resistance to hypotonic salt solution; abnormal blood smears as evidenced by the presence of oval and target cells, a high number of cells with basophilic stippling, an occasional nucleated red cell, and an increased number of reticulocytes; positive x-ray changes of the femurs; Mediterranean racial factor with familial trait as shown by the increased resistance to hemolysis in hypotonic solution of the blood of one sister with hypochromic microcytic anemia; lack of sickling of red cells; and the absence of chronic bleeding, hepatic disease, steatorrhea, or lead poisoning. The

TABLE I

DATE	RED BLOOD COUNT (MILLIONS PER CUBIC MILLI- METER)	HEMO- GLOBIN (GM. %)	HEMA- TOCRIT (%)	MEAN CORPUS- CULAR VOLUME (CUBIC MICRON)	VOLUME INDEX	COLOR INDEX	MEAN CORPUS- CULAR HEMO- GLOBIN (MICRO- MICRO- GRAM)	MEAN CORPUS- CULAR HEMO- GLOBIN CONCEN- TRATION (%)
Nov. 10, 1944	4.06	8.2	36.0	88	1.01	0.69	20.20	22.8
Dec. 8, 1944	3.21	6.6	--	--	--	0.71	20.56	--
Dec. 14, 1944	3.97	8.3	27.2	68	0.79	0.72	20.90	30.5
Dec. 29, 1944	3.76	8.2	31.9	85	0.98	0.75	21.80	25.7
Jan. 26, 1945	4.10	8.8	21.4	52	0.60	0.74	21.46	41.1
Feb. 2, 1945	4.26	8.0	24.0	56	0.64	0.65	18.77	33.3
Feb. 16, 1945	4.31	8.0	26.1	60	0.69	0.64	18.56	30.7
Mar. 2, 1945	4.06	8.0	26.2	64	0.74	0.68	19.07	30.7
Mar. 26, 1945	3.65	6.8	24.0	66	0.76	0.64	18.63	28.3
Mar. 30, 1945	3.95	6.9	--	--	--	0.61	17.56	--
Apr. 2, 1945	4.02	6.2	24.7	61	0.70	0.53	15.42	25.1
Apr. 17, 1945	3.20	6.6	20.4	64	0.74	0.71	20.63	32.3
May 10, 1945	3.87	6.6	26.0	67	0.77	0.59	17.05	25.4
May 24, 1945	3.93	7.0	--	--	--	0.61	17.81	--
June 1, 1945	3.92	7.5	--	--	--	0.66	19.13	--
June 7, 1945	4.12	7.3	--	--	--	0.61	17.72	--
June 14, 1945	3.83	7.5	--	--	--	0.68	19.59	--
July 3, 1945	4.63	8.8	29.6	65	0.76	0.65	19.00	29.7
July 7, 1945	Delivery	--	--	--	--	--	--	--
July 7, 1945	4.42	8.8	--	--	--	0.69	19.91	--
July 9, 1945	4.55	9.2	--	--	--	0.70	20.22	--
July 15, 1945	4.31	10.5	33.0	77	0.88	0.84	24.36	31.9
Aug. 14, 1945	5.10	10.2	30.3	59	0.68	0.69	20.00	33.6

All were noted throughout the course, with stippling occurring in 3.4 per cent of the cells on one occasion. Sickling test using carbon dioxide method was negative on two occasions. Icterus index varied between 7.0 and 16.0 on seven determinations. Van den Bergh indirect varied between 2.0 mg. per cent and 3.53 mg. per cent. Serum protein three weeks before delivery when weight gain was taking place was 7.43 mg. per cent. At this same time serum albumin was 3.70 mg. per cent and serum globulin was 3.73 mg. per cent, giving an albumin globulin ratio of 0.99. Platelets were normal on four determinations as were the bleeding and clotting times, nonprotein nitrogen, blood uric acid, and cold agglutinin tests. Red corpuscle fragility tests on two occasions are shown in Table II.

TABLE II. RED CORPUSCLES FRAGILITY TESTS ON PATIENT

	A) PATIENT	CONTROL	(B) PATIENT	CONTROL
Partial hemolysis	0.42%	0.44%	0.36%	0.42%
Complete hemolysis	0.30%	0.36%	0.28%	0.38%

Urine: Negative on all routine examinations. Urobilinogen 4+ found on one occasion but urobilin and bile acids negative at this time. No hemosidrin granules found. Stool: Negative for blood and parasites. Gastric analysis: December, 1944, Ewald test meal: total acid 15.6, free acid none. March, 1945, alcohol stimulation: total acid 7.0, free acid none. July, 1945 (postpartum), histamine stimulation: total acid 60, free acid 48. Basal metabolism rate, +6 and +9.

X-rays: X-ray examination of the femurs revealed decreased width of the cortex in the lower fourth with rarefaction and thinning of the bony trabeculae. Characteristic of chronic anemia. The hands and skull were normal.

## PELVIC ENDOMETRIOSIS AS A CAUSE OF HYDRONEPHROSIS\*

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THE literature contains many references to pelvic conditions causing obstructive lesions of the upper urinary tract. Among those commonly described are pregnancy, carcinoma of the cervix, uterine prolaps with cystocele, fibromyomas, ovarian growths, and salpingitis. Reports on the effect of pelvic



Fig. 1.

\*Presented before the meeting of the Chicago Gynecological Society, March 15, 1946.

anemia regressed moderately at the end of pregnancy as does the "physiologic anemia of pregnancy." The over-all picture appears to be a benign Mediterranean anemia with a "physiologic anemia of pregnancy" superimposed upon it.

Regarding the transfusion reaction, it is known that reactions are more prone to occur in the group of chronic hemolytic anemias.<sup>7</sup>

Our treatment helped diagnose the type of anemia, but following diagnosis it was without proof of benefit. We do not know what would have happened had we given no iron at all, but suspect the anemia may have been more pronounced. For this reason it was continued in large doses.

In considering cases of adult Mediterranean anemia, it must be remembered that these patients are not as severely affected as are the childhood cases. Consequently, the changes in the blood, bones, and spleen are not as marked. Diagnosis in these cases is much more difficult, and in borderline cases more open to criticism.

### Conclusion

A case of adult type Mediterranean anemia observed and diagnosed while the patient was pregnant has been presented. Treatment of the anemia following diagnosis was by large doses of iron, although there is no proof of its efficacy. This diagnosis must be considered in cases of obscure anemia, especially in patients of Italian descent.

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Miss G. W., a 31-year-old nulliparous Negro woman, entered the gynecologic service on Nov. 27, 1945, complaining of progressively increasing dysmenorrhea for the past six years. During this time the menses recurred every twenty-one days with pain across the lower abdomen, especially marked in the left flank. The pain was associated with nausea and vomiting. Previously, the menses recurred every twenty-eight days and were painless. General physical examination was essentially negative. Rectovaginal examination revealed an irregularly enlarged uterus the approximate size of a six weeks' gestation, hard and fixed in retroversion. In the cul-de-sac and along the uterosacral ligaments were multiple small, hard, fixed tender masses. In the right adnexal region and adherent to the uterus was a firm tender mass. The left adnexae were not palpated. A diagnosis of fibroid uterus and endometriosis was made. Laparotomy was performed on Dec. 1, 1945. The uterus was bound down posteriorly by dense fibrous adhesions. The right-sided mass was a large "chocolate" cyst of the right ovary adherent to the posterior surface of the right broad ligament by dense adhesions. The left tube and ovary were also bound to the left broad ligament by dense adhesions. After liberating the adnexae and freeing the uterus, it was found that the upper rectovaginal septum was markedly infiltrated. The peritoneum of the cul-de-sac and the anterior surface of the rectum were studded with endometriomatous nodules and the entire posterior wall of the uterus, cul-de-sac, and anterior rectum presented a raw, oozing surface. The ureters were markedly dilated and descended in an unusual position along each side of the rectum and disappeared into the dense endometriomatous mass medial to the uterosacral ligaments. Total hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus was removed by opening into the anterior vaginal vault first and then detaching it posteriorly by sharp dissection from the posterior fornix upwards in order to avoid the ureters. Because of the multiple raw surface, peritonealization was accomplished by constructing a "pelvic diaphragm" with the sigmoid sewed to the reflected bladder peritoneum. The extraperitoneal space thus produced was drained through the vagina. On December 8, the seventh postoperative day, intravenous pyelography revealed marked hydroureter and hydronephrosis (Fig. 1). The patient made an uneventful convalescence and was discharged on the eighteenth postoperative day. Intravenous pyelography on Feb. 4, sixty-five days after operation, revealed a return to a normal status of the upper urinary tract (Fig. 2).

The above case illustrates slow constriction of the ureters by endometrioma of the pelvic peritoneum and rectovaginal septum. The ureters in this case were displaced medially. Bilateral hydroureter was demonstrated at operation. An intravenous pyelogram taken seven days following total hysterectomy and bilateral salpingo-oophorectomy showed bilateral hydroureter and hydronephrosis. Follow-up excretion pyelography taken sixty-five days after operation showed a return of the upper urinary tract to a normal status. Cure of the urinary tract pathology was effected by shrinkage of the endometriomatous infiltration after removal of the ovarian stimulation.

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endometriosis on the ureter are rare. Randall, in 1941, reported a case of primary involvement of the ureter by endometrioma. O'Connor and Greenhill, in 1945, reported the second case of intraureteral endometrioma, and Goodall reported four cases of ureteral involvement. In two of the latter cases death was due to uremic poisoning following profound hydropyonephrosis. Autopsy findings in one of these cases revealed invasion of the lower ureteral walls by the endometrioma so that the lumina were almost completely occluded, though nowhere was the mucosa invaded.

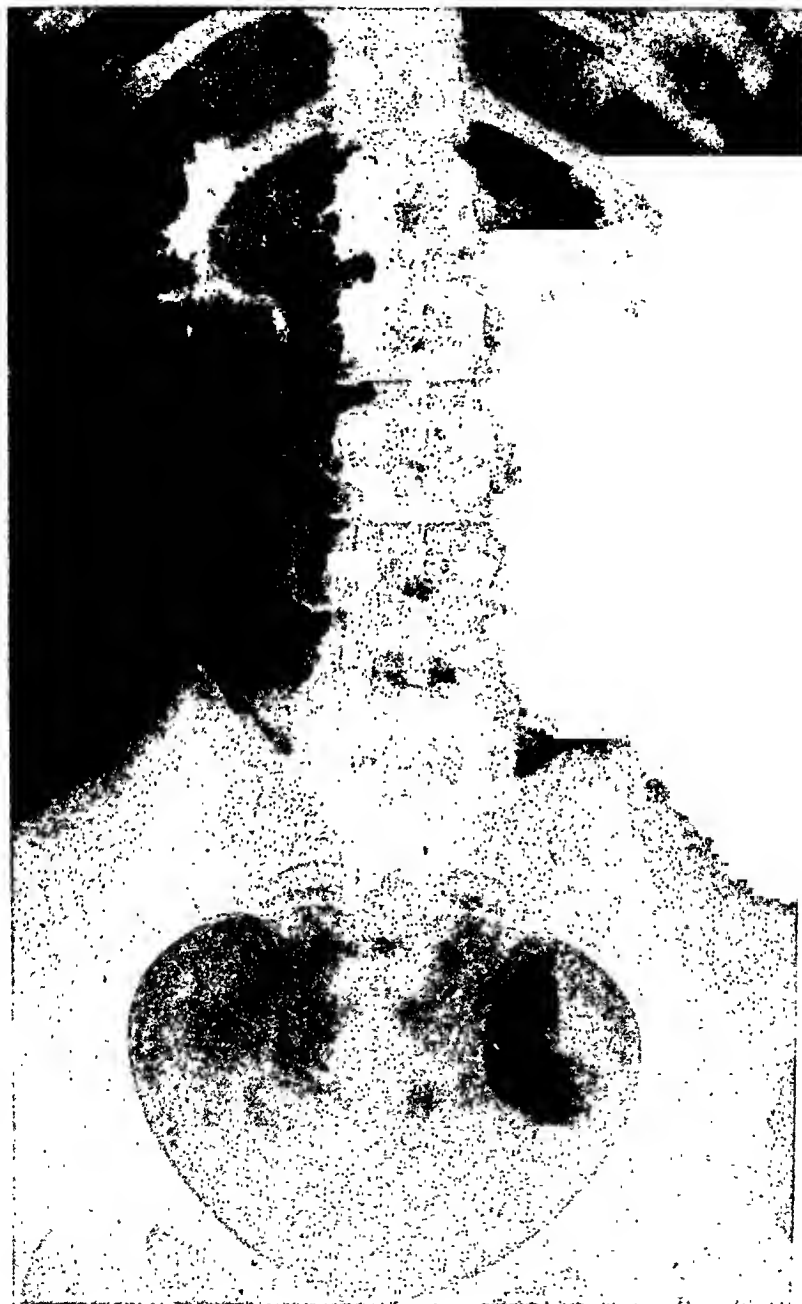


Fig. 2.

The following case report demonstrates constriction of the ureters by pelvic endometriosis with resultant hydroureter and hydronephrosis. This constriction, demonstrated roentgenologically, was released after removal of the instigating cause of the endometriomatous growth, namely, the ovarian secretion.

**Kaeser, O.:** Pregnancy and Rupture in the Scar Area After Salpingectomy With Excision of the Cornu Because of Interstitial Pregnancy, *Monatschr. f. Geburtsh. u. Gynäk.* 195: 7, 1943.

The author reports a case of ectopic pregnancy and rupture in the scar area after wedge excision of the cornu for interstitial pregnancy. The fetus escaped into the abdominal cavity at the beginning of the eighth lunar month. It was delivered alive by laparotomy but failed to survive. In this case there were no signs of rupture such as internal hemorrhage and peritoneal shock. The author suggests that in certain cases of interstitial pregnancy, prophylactic tubal sterilization should be performed. J. P. GREENHILL.

**Howard, G. Turner, Jr.:** Simultaneous Ruptured Tubal Pregnancy and Intrauterine Pregnancy With Subsequent Delivery of a Normal Infant, *South. M. J.* 38: 788, 1945.

A third case of simultaneous intrauterine and extrauterine pregnancy is added by Howard to two others found previously reported. Five weeks prior to hospitalization, the patient had a normal menstrual cycle, followed in one week by intermittent cramp-like pains with brownish vaginal discharge. Pain finally localized in the left lower quadrant, and the patient was hospitalized. On admission, examination revealed a uterus of grapefruit size, smooth and soft, with thickening in the left vaginal vault. Temperature was 99.4° F., white blood cell count, 12,100, moderate anemia. Sharp pain in the left lower quadrant, with tenderness and spasm, developed eighteen hours after admission. Laparotomy, done on this indication, revealed a ruptured ectopic in the left tube, and a uterus the size of a two and one-half months' pregnancy. A positive Friedmann test was reported eleven days postoperative, and the patient delivered a normal infant seven months later. JEROME SHAPIRO.

## Gynecology

**Hundley, J. Mason, and Diehl, William K.:** The Influence of Gynecologic Disorders on the Urinary System, *J. A. M. A.* 127: 572, 1945.

The various normal physiologic changes occurring in the urinary tract with pregnancy are reviewed. The two chief changes on the ureteral tract are pressure changes and hormonal activity on ureteral atony. The effects of tumors, both benign and malignant, are mentioned. The urinary complications resulting from parturition are chiefly cystocele and decensus. Inability to empty the bladder results in stasis with chronic infection and cystitis. Stress incontinence is another complication resulting either from obstetric trauma or in the postmenopausal patient. Operative repair of these conditions is described. Although vesicovaginal fistulas are rarer these days with improved obstetrical care, an occasional case arises which necessitates repair. The authors describe their procedure for the repair of a large vesicovaginal fistula.

One of the commonest causes of ureteral involvement is due to chronic adnexal disease. Hydroureter and hydronephrosis are not uncommon complications of chronic salpingitis. The authors do not feel that endocervicitis plays a role in the production of cystitis and trigonitis. Endometriosis of the bladder is mentioned as an uncommon complication. The treatment of choice is mentioned in many of these urinary complications.

WILLIAM BERMAN.

**Müller, J. H.:** The Question of Tubal Peristalsis, *Monatschr. f. Geburtsh. u. Gynäk.* 117: 300, 1944.

The author presents hysterosalpingograms to prove that tubal peristalsis exists. His x-ray pictures revealed both tubal peristalsis in the direction of the uterus and peristaltic action from the uterine end toward the fimbria. In the author's two cases of sacrosalpinx, the iodine masses moved from place to place, showing that both peristalsis and antiperistalsis took place, producing an alternating peristalsis. J. P. GREENHILL.

# Department of Reviews and Abstracts

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## Selected Abstracts

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### Cancer, Malignancies

Daland, Ernest M.: Some Unusual Aspects of Cancer of the Breast, *New England J. Med.* 233: 515, 1945.

The author gives a concise summary of the contributions of outstanding surgeons leading to the radical breast mastectomy for carcinoma. Early diagnosis and treatment are essential for the cure in breast cancer. Vague symptoms in the breast, deformity, and lumps must be investigated by biopsy.

Exceptions may be made to performing the radical operation in certain cases, such as sepsis in the cancer, old age, or poor physical condition. Occasionally, but rarely, a five-year survival is obtained by this procedure. Three cases of cancer of the breast in girls under nineteen are reported.

JAMES P. MARR.

Brooke, Wallace S., and Thomason, J. R.: Leiomyosarcoma of the Uterus With Metastasis to the Femur, *Arch. Surg.* 51: 120, 1945.

The authors deal with sarcoma of the uterus, reporting such a case. Metastases from sarcoma of the uterus are most common in the lungs, peritoneum, lymphnodes, liver, and kidneys. Little has been written concerning metastases of uterine sarcomas to the bone, such as the authors report.

JAMES P. MARR.

Recasens Mendez—Queipo de Llano, M.: A Case of Probable Spontaneous Healing of a Chorionepithelioma, *Rev. espan de obst. y ginec.* 2: 86-88, 1945.

In the treatment of an incomplete abortion in a 21-year-old patient, chorionepithelioma was diagnosed and radium treatment applied for forty-eight hours. Through accidental circumstances, the x-ray treatment which was to follow was delayed; and when the patient was examined three months later and subsequently, normal function had been restored, and all evidence of the cancer had disappeared.

J. P. GREENHILL.

### Extrauterine Pregnancy

Clerc, J. P.: Errors in the Diagnosis of Ectopic Pregnancy, *Monatsschr. f. Geburtsh. u. Gynäk.* 118: 169, 1944.

The author analyzed eleven cases where errors in the diagnosis of ectopic pregnancy had been made. In four cases the ectopic gestations were not recognized and, in the remaining seven cases, ectopic pregnancy was diagnosed in the presence of other conditions. The author emphasizes that in ectopic pregnancy the symptoms are not characteristic. Of the 25 tubal pregnancies operated on every year at the Geneva Obstetric and Gynecologic Institute, errors are made in three or four cases. In doubtful cases exploratory procedures should be carried out. In the four cases erroneously diagnosed in the Clinic, the correct diagnosis was made by means of pelvic puncture.

J. P. GREENHILL.

Pali, K.: Conduct of Labor in the Presence of Thrombosis, *Monatsehr. f. Geburtsh. u. Gynäk.* 119: 34, 1945.

If in cases of venous thrombosis there exists a contracted pelvis, placenta previa, transverse presentation, advanced age in a primipara, breech presentation with premature rupture of the bag of waters, large baby, eclamptic convulsions, tumors preventing vaginal delivery, edema of the vulva, etc., cesarean section is necessary. In general, the conduct of labor in the presence of a thrombosis depends on whether the patient is a primipara or a multipara. Likewise, the site of the thrombosis and the phase of development of the thrombosis are important.

J. P. GREENHILL.

Dominguez Sisco, R., and Agüero, O.: Manual Extraction of the Placenta and Hydraulic Injection, *Rev. de obst. y ginec.* 5: 17, 1945.

The authors analyzed their cases of manual removal of the placenta and compared the results with a series of cases in which they used injection of saline solution into the umbilical cord for release of the placenta. Among 282 cases of manual removal of the placenta puerperal infection occurred in 43 per cent, and the death rate was 1.77 per cent. Among the 60 cases where the Mojon-Gabastou injection technique was used, puerperal infection occurred in 2.27 per cent and there were no maternal deaths. Hence the authors favor the injection method, and they recommend a modification of it.

J. P. GREENHILL.

### Miscellaneous

Peters, Hannah, and Foster, Wilson: Gynecology in Industry. Causes, Treatment, and Educational Program, *Indust. Med.* 14: 755, 1945.

The authors summarize two years' experience in the Gynecology Clinic of the Permanent Foundation Hospitals which had served a group of women comprising as many as 23,000 at one time in the shipyards in the Richmond area.

Menorrhagia and metrorrhagia did not appear to show any correlation with the type of work undertaken by the women, save at the outset when women began heavy labor. There was no evidence that hard work, standing, or walking for eight hours caused menstrual disorders. The welding arc exhibits no influence on the catamenia. Sealing and clipping produced no untoward disorder in the menses. The authors explain the increase of menorrhagia concurrent with the onset of heavy labor to dietary changes. Before these women started to work they were eating at best a diet low in vitamin B complex. When manual labor was initiated their caloric requirement and intake became greater. In compensation, they utilized more and more carbohydrates which require more vitamin B complex, which they did not get. The deficiency in Vitamin B complex became progressively greater. Therapy with the B complex controlled the majority of these cases exhibiting menorrhagia and hypermenorrhea with the onset of heavy labor. The writers have not completed their review of those cases with pelvic inflammatory disease. They do state that some cases given an older history of inflammatory disease did present themselves with bleeding, pain, and symptoms of acute exacerbation after a period of heavy work.

The authors state they tried to find a cause for abortion in working women but—"in not a single case could the type of work be held responsible for the early termination of pregnancy." The writers gave no figures to indicate the incidence, type, course, or treatment of women aborting while employed in industry. They agree that the policy of discharging a woman as soon as it becomes known she is pregnant is certainly a hazardous policy.

The medical education program was concerned with a twofold objective, cancer detection, and venereal disease education. All women were subjected to the older Schiller's Iodine Test. Cancer of the ovaries, uterus, and the cervix amounted to 0.9 per cent of all the new cases in these hospitals. Thirteen per cent of all the new gynecologic cases were found to be infected with gonorrhea.

It is unfortunate the authors neglected to mention the number of patients seen presenting the various gynecologic diagnoses. By the omission of such numbers and their statistical evaluation, much of the significance of this valuable data from these large clinics is lost for clinical specialty consideration.

CLAIR E. FOLSOME.

Kese, G.: *Leech Treatment in Obstetrics and Gynecology*, Monatschr. f. Geburtsh. u. Gynäk. 117: 306, 1944.

In order to study the effect of leeches, the author examined the blood of healthy obstetric patients who had been operated on and women with thrombosis as regards the bleeding time, coagulation time, and prothrombin values. A definite prolongation in coagulation and bleeding time was found only in the local oozing blood, but there was no alteration in the prothrombin values. The good results obtained following treatment with leeches is explained by the local withdrawal of blood thereby eliminating pain and the sense of tension. There is also a decrease in the amount of edema and lymph congestion due to improvement in the lymph and collateral circulation. Leech therapy decreases the time of healing. Although it is not understood how the hirudin in the living leech acts, ten years' experience leads the author to recommend strongly the prophylactic and therapeutic use of leeches after every obstetric and gynecologic operation. J. P. GREENHILL.

Scheidegger, S.: *The Question of So-called Granulosa- and Theca-Cell Tumors of the Ovary*, Monatschr. f. Geburtsh. u. Gynäk. 114: 175, 1942.

From an experience with four cases in women 6, 52, 75, and 82 years of age, the author came to the conclusion that there are transition forms between the classical granulosa-cell tumors and theca-cell tumors. Pure granulosa-cell tumors are extremely rare. In most cases of granulosal neoplasms, typical theca-cell formations may be found. Sometimes the granulosa- and sometimes the theca-cell formations predominate. It is impossible to make a sharp differentiation between the two types of tumors. J. P. GREENHILL.

### Labor, Management, Complications

Ascanio, Escobar R.: *Breech Presentation in the "Concepcion Palacios Maternity,"* Rev. de obst y ginec. 5: 5, 1945.

The incidence of breech presentation at the "Concepcion Palacios Maternity" was 3.4 per cent. Premature babies constituted more than one-third of the babies, and more than two-thirds of the patients were multiparas. The duration of labor was within normal limits. The total fetal mortality was 30.9 per cent and the corrected rate was 7.1 per cent. The most frequent complications during delivery were prolapse of the cord and lacerations of the genital tract.

The author recommends routine version during pregnancy by means of laxatives and enemas. If these fail, manual external version should be tried. An experienced physician should aid the breech extraction in order to reduce the fetal mortality. Forced traction on the head should be avoided in order to lessen intracranial lesions. Episiotomy should be employed more frequently in multiparas as well as in primiparas, especially in the presence of premature babies. The increased use of forceps on the aftercoming head will avoid the dangers of the Mauriceau maneuver. As parts of the instrumentarium, vaginal retractors and an electric aspirator should be included. J. P. GREENHILL.

Biro, S.: *Labor in Overweight Women*, Monatschr. f. Geburtsh. u. Gynäk. 117: 185, 1944.

The author studied a series of 160 overweight pregnant women observed over a period of six years. He found that these women had a greater incidence of toxemia and malpresentations of the fetus. The children were larger than usual, their average weight amounting to 3,698 grams. Almost one-fourth of the babies weighed more than 4,000 grams. Labor was not prolonged in these cases but uterine atony, puerperal infection, and operative interference were more frequent. The death rate was 2.5 per cent. These facts indicate that overweight pregnant women require special attention. J. P. GREENHILL.

Leonard, Martha F.: Hemolytic Disease of the Newborn (Erythroblastosis Fetalis) Clinical Analysis of Fifty-Five Cases, With Special Reference to Pathogenesis, Prognosis, and Therapy, *J. Pediat.* 27: 249, 1945.

Fifty-five cases of hemolytic disease of the newborn treated at the New York Hospital are reported.

In thirty-three cases, Rh factors were determined; of these, 84 per cent showed the typical pattern. In 16 per cent mother, father, and infant were all Rh positive. These figures are consistent with observation of others. The pathogenesis of hemolytic disease of the newborn has not yet been completely elucidated. The factor of isoimmunization has been generally accepted, and needs no repetition. Recent authors have stressed hemolysis as the primary factor, with other manifestations as secondary to the hemolysis and the accompanying anemia.

Impaired ability of the liver to form prothrombin has been amply demonstrated by autopsy findings in 9 patients showing liver damage with necrosis, fatty degeneration, vacuolation, or unusual pigment accumulation. A number of explanations have been advanced for the cause of this poor liver function, as: intrauterine asphyxia due to placental abnormality or to drugs given the mother during labor, or immaturity, constitutional inferiority, or anaphylaxis.

Recovery from the disease required from one week to three months. The tendency for anemia to recur often lasted as long as from four to six weeks after birth, necessitating repeated transfusions. Nineteen of the 55 infants died, a mortality of 35 per cent.

The prominence of hemorrhagic tendencies in patients with hemolytic disease of the newborn was emphasized, and the value of vitamin K given to the mother or infants are demonstrated.

The necessity for immediate transfusion in the presence of normal blood levels are questioned, and reasons were given for delaying transfusion until anemia impends. Plasma infusions were preferred in this type of patient.

Administration of vitamin K to donors of Rh-negative blood was suggested as a means of raising the prothrombin levels of affected patients.

JAMES P. MARR

Miller, Herbert C.: The Effect of the Prediabetic State on the Survival of the Fetus and the Birth Weight of the Newborn Infant, *New England J. Med.* 233: 376, 1945.

The nature of the factor or factors responsible for the increased newborn mortality and increased birth weights of infants born to prediabetic mothers remains unknown. Presumably, the primary factors are the same as those that are responsible for the high mortality and increased birth weight of infants born to mothers who already have developed diabetes.

Because obesity is one of the frequent characteristics of women developing diabetes in later life, and because it seemed possible that the maternal obesity was a factor in the increased birth weights, a study of such material was made, and the conclusion drawn that there was no significant difference found between the average birth weight of the infants in the obese group and those in the nondiabetic group.

JAMES P. MARR

### Pregnancy, Complications

Brentnall, C. Philip: A Case of Arrhenoblastoma Complicating Pregnancy, *J. Obst. & Gynaec. Brit. Emp.* 52: 235, 1945.

The author reports this rare case occurring in a pregnancy in which the mother showed all the external evidence of masculinization. She was delivered by cesarean section after spontaneous rupture of her membranes during the thirty-seventh week of pregnancy, and was delivered of a 6½-pound child resembling a female pseudohermaphrodite.

An attempt is made by the author to explain the embryologic development of the child with reference to the appearance of the external genitalia, and he concludes that it is most

**Tompkins, Pendleton:** Basal Body Temperature Grasps as an Index to Ovulation, *J. Obst. & Gynaec. Brit. Emp.* 52: 241, 1945.

Evidences are accumulating that the basal body temperature in women is directly related to the phases of the menstrual cycle. The temperature is relatively low prior to ovulation, shifts to a higher level about the time of ovulation, and maintains this higher level until the next menses, when it falls and the cycle is then repeated. This study is important in the evaluation of infertility. Reasonable care must be employed to insure basal conditions when the temperature is taken. All temperatures were taken by rectum and were taken in the morning before arising and before taking food or liquid. A number of charts illustrating the above are included in the manuscript. WILLIAM BERMAN.

**Schneider, Wilnot F.:** Arachnodactyly—Unusual Complication Following Skull Injury, *J. Pediat.* 27: 583, 1945.

This report traces the progressive development of various anomalies observed in Marfan's syndrome. In the reported case failing vision was definitely observed between the fourth and fifth year. Progressive loss of vision finally shut the girl from the world almost completely. She was not adequately safe-guarded. At the age of 12 years she fell through an open cellar door and had her visual abnormalities complicated by the head injury, which set in motion the retinal detachment and bilateral glaucoma. The author recommends early orthopedic treatment to prevent crippling deformities, and early recognition of ocular deficiencies and treatment. JAMES P. MARR.

### The Newborn

**Wespi, H. J.:** Reduction of Deafness and Dumbness in Switzerland as Result of Goiter Prophylaxis With Iodized Salt, *Schweiz. med. Wchnschr.* 75: 625, 1945.

During the years 1915 to 1922 the incidence of deafness and dumbness varied between 11.7 and 16.6 per 10,000 live born children. After 1922 the incidence decreased so that as early as 1925 the figure was 4.3 per 10,000 live births. This reduction in deafness and dumbness occurred simultaneously with the introduction of iodized salt into Switzerland. Even in the cantons which had as high an incidence as 20 per 10,000 cases of deafness and dumbness experienced a rapid drop in the incidence after the introduction of iodized salt. Hence, there is a definite connection between goiter prophylaxis and reduction in the frequency of deafness and dumbness. J. P. GREENHILL.

**Wespi, H. J.:** The Prevention of Goiter in the Newborn, *Monatschr. f. Geburtsh. u. Gynäk.* 118: 113, 1944.

The author administered an iodine solution in addition to iodized salt to pregnant women, and thereby reduced the incidence of goiter in the newborn babies. The frequency of goiter in the newborn was inversely proportionate to the amount of iodine administered. Hence goiter is primarily an iodine deficiency disease and can be prevented by giving iodine. J. P. GREENHILL.

**Graubarth, Julian, Bloom, Charles J., Coleman, Francis C., and Solomon, Harry N.:** Dye Poisoning in the Nursery, *J. A. M. A.* 128: 1155, 1945.

The authors report 17 cases of aniline poisoning that occurred in a nursery where the diapers were stamped with ink containing aniline dye. Thirteen babies recovered, and four died from unrelated causes. This condition is to be differentiated from other causes of cyanosis in a newborn. These babies were treated with methylene blue, oxygen with 5 per cent carbon dioxide and whole blood transfusions. The methylene blue and oxygen had no apparent effect on the time and type of recovery of any of the infants. Adequate treatment lies first in the prevention, then in removing the source, transfusion of whole blood or red cells suspended in saline solution, fresh air, and isolation. WILLIAM BERMAN.



If a hemorrhage occurs when the patient is approaching term, e.g., at thirty-eight weeks, the treatment indicated can be carried out immediately. This plan has resulted in the reduction of infant mortality. In the first 47 cases in which this plan was not in force, the average weight of the infants at birth was 5 pounds, 2 ounces, and the infant mortality was 47 per cent; while in the last 47 cases, the average weight of the infants at birth was 6 pounds, 12 ounces, and the infant mortality 6 per cent.

It has long been recognized that a placenta previa is usually larger and thinner than normal; it has also been recognized that in placenta previa there is often an eccentric insertion of the umbilical cord. The importance of the latter fact, the author believes, has not generally been recognized in its relation to fetal mortality. If the cord is inserted at the lower edge of the placenta where the separation occurs, or has a velamentous insertion in this area, the infant often dies after the initial hemorrhage, although this is not severe; while if the cord is inserted centrally or at the edge of the placenta farthest away from the internal os, the infant survives even though the hemorrhage is more severe.

In case of type I placenta previa, artificial rupture of the membranes is usually sufficient to control the hemorrhage. This was the method employed in 38 of 50 cases of this type in this series; only two cesarean sections were done in this group, both in elderly patients. Version has been used chiefly for controlling severe hemorrhage when the fetus is immature or has died; it can also be used for delivering a multipara with a history of very rapid deliveries, when the infant is full term and living. Cases of type II on the anterior wall can usually be treated by artificial rupture of the membranes; but if situated posteriorly cesarean section is often indicated. Cesarean section is also the safest method in cases of type IV and in most cases of type III. Cesarean section was done in 68 cases in this series, with a fetal mortality of 2.9 per cent (2 deaths). The majority of cesarean sections were of the lower segment type, especially in the later years. The danger of hemorrhage in this type of operation is diminished by the injection of 0.25 mg. of ergometrine and 1 c.c. of pitocin into the uterine wall, and the removal of the placenta after the uterine incision has been partially sutured.

HARVEY B. MATTHEWS.

### Pregnancy, Physiology

Braga, E.: Clinical Sign Diagnostic of Early Pregnancy, *Obst. y ginec. latino-am.* 3: 321, 1945.

The author presents a new sign of early pregnancy. In a series of 1,110 primiparas between 16 and 26 years of age he found it in 98.5 per cent up to the second week of pregnancy(?). It then disappeared slowly after this time. The sign consists of the ability to produce with the two examining fingers a fold of vaginal mucosa on either side of the cervix. The slow and progressive disappearance of the fold demonstrates the gestational imbibition of the cervix. The sign is called the "Supplementary Hegar" sign in honor of Hegar, and also to indicate that it is a substitute for the Hegar No. 2 sign which is a dangerous procedure.

J. P. GREENHILL.

Kendrick, Pearl, Thompson, Mary, and Eldering, Grace: Immunity Response of Mothers and Babies to Injections of Pertussis Vaccine During Pregnancy, *Am. J. Dis. Child.* 70: 25, 1945.

The authors report the results of their study on the opsonocytophagic reaction of *H. pertussis* of 99 pregnant women, of whom 57 were immunized with pertussis vaccine, and 42 were nonimmunized.

From a practical standpoint, the results of the study suggest the value under certain conditions of giving a series of injections of pertussis vaccine to pregnant women to raise the level of immunity in their babies.

JAMES P. MARR.

Vartan, C. Keith: The Behaviour of the Foetus in Utero With Special Reference to the Incidence of Breech Presentation at Term, *J. Obst. & Gynaec. Brit. Emp.* 52: 417, 1945.

In a study of 3,875 pregnant women in an antenatal clinic, the author found that the fetus was in breech presentation at some time during the pregnancy in 1,000 cases. The first

likely that the androgen from the ovarian tumor did not reach the fetus in effective quantity until the third month of fetal life, and by this time the female hormone of the fetal gonad had already produced some reactions in the accessory sex organs, probably in the upper part of the urogenital sinus.

WILLIAM BERMAN.

Beacham, Woodward Davis, and Varino, George Andrew: Ruptured Uteri: An Analytical Report of Sixty-Four Cases Managed at the Charity Hospital of Louisiana at New Orleans, With a Review of the Literature, New Orleans M. & S. J. 98: 91, 1945.

The authors' analytical report on 64 cases of ruptured uteri includes a short history and a survey of the incidence, mechanism, etiology, pathology, diagnosis, and treatment of this obstetric emergency. The significant factor is a diagnosis prior to rupture, this being determined by no progress in labor, despite strong and frequent pains and impending or actual rupture by tenderness over the lower segment, and sudden, sharp, tearing pain in the abdomen. Statistics are quoted, giving the fetal and maternal mortality from various sources, the fetal mortality being in the authors' series 73 per cent and 60.9 per cent, respectively. Interesting factors mentioned are frequency of rupture in the classical as compared to low flap sections, the importance of proper scar healing in previous sections, and the prophylactic measures stressed: namely, avoidance of oxytocics, and early cesarean section.

The thought occurs that some of these cases may have been put into further shock after transfusion, and the value of determination of the Rh factor in all of these cases prior to this transfusion is suggested.

The bibliography following the article is an excellent source for further reading on this subject.

JEROME SHAPIRO.

James, David W.: Pernicious Vomiting of Pregnancy Due to Sensitivity to Semen, West. J. Surg. Obstetrics and Gynecology 53: 380, 1945.

This case, apparently the first reported of pernicious vomiting of pregnancy due to contact sensitivity to the husband's semen, revealed several interesting facts. During each of three attacks, the vomiting occurred exactly three days after intercourse with semen deposition; each attack subsided after eight days. There was no response to the usual therapeutic measures, such as sedation, thiamine intravenously, isolation, restricted diet, and bed rest. Coitus, using a condom, and coitus interruptus produced no allergic phenomena. Passive transfer, by injecting the patient's serum into three nonallergic individuals, demonstrated the patient's sensitivity to an extract of her husband's semen.

JEROME SHAPIRO.

Macafee, C. H. G.: Placenta Previa—A Study of 174 Cases, J. Obst. & Gynaec. Brit. Emp. 52: 313, 1945.

In a series of 174 cases of placenta previa treated at the Royal Maternity Hospital in 1937 to 1944, and including 23 private cases, there was only one maternal death (maternal mortality, 0.57 per cent); the fetal mortality (stillbirths and neonatal deaths) was 23.5 per cent (41 deaths). In the earlier cases in this series, vaginal examination was made in many cases shortly after admission to the hospital; 17 of the 91 fetal deaths occurred in the first two years. In the later years vaginal examination was not made until all preparations were made for carrying out the subsequent treatment indicated. A vaginal examination was ultimately made in every case in this series to determine the type of placenta previa and the best method of treatment. But the author's experience has convinced him that placenta previa is not an emergency that must necessarily be dealt with at the first hemorrhage; severe initial hemorrhage rarely occurs unless vaginal examination is made; and such examination should, therefore, be postponed to as near full term as possible, when the patient is prepared for delivery by cesarean section, if necessary. Several patients in this series have remained in the hospital for weeks and have had repeated small hemorrhages before vaginal examination was made. This plan avoids one of the chief dangers to the fetus—prematurity.

of a special apparatus which they devised. Previously the authors reported a series of 80 cases in which they used sulfanilamide prophylactically and in which the incidence of morbidity was only 5 per cent. They now add 65 cases. These 145 women had been subjected to various types of obstetric operations, some of them serious; yet morbidity occurred in only 11 per cent. The authors firmly believe that prophylactic local chemotherapy during obstetric operations marks a real advance in obstetric progress.

J. P. GREENHILL.

Bird, J. G.: Postpartum Traumatic Gynatresia, *Bol. Asoc. méd. de Puerto Rico* 37: 205, 1945.

The author operated upon a woman who had a complete traumatic atresia of the vagina following a forceps delivery ten years previously. After making a new vagina, a vaseline gauze tampon was used because the author could not obtain a rubber plug. Two months after operation, the vagina permitted the insertion of three fingers and also a moderate-sized speculum without any pain. Coitus could be performed without discomfort. Three months later the patient was pregnant. In a second case of partial stenosis following a forceps delivery constriction rings were incised laterally and sutured vertically with excellent results. There has been no dyspareunia since the operation.

J. P. GREENHILL.

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## Item

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### American Board of Obstetrics and Gynecology, Inc.

#### Examinations

The next written examination (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 7, 1947, at 2:00 P.M. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination held later in the year. All applications must be in the office of the Secretary by Nov. 1, 1946. Candidates in military service are requested to keep the Secretary's Office closely informed of changes in address.

A number of changes in Board regulations and requirements were put into effect at the last annual meeting of the Board held in Chicago, Illinois, from May 5 to May 11, 1946. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. At this meeting the Board also ruled that it will not accept the nine months' residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration, April 1, 1946.

Applications are now being received for the 1947 examinations. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

PAUL TITUS, M.D.

examination for this particular study was made at about the thirtieth week of pregnancy. If it had been possible to make repeated skiagrams of all cases, an even higher incidence of breech presentation might have been found. In 680 cases spontaneous cephalic version took place, and in 599 of these cases this was the only movement of the fetus known to have taken place. Spontaneous version was observed to take place at a specific time in pregnancy; in this series by the thirty-fourth week, and probably in many cases by the thirty-second week. The incidence of reversion to the breech presentation was low (25 cases). External version was performed in 330 cases; in 223 cases this procedure was successful and no reversion occurred; in an additional 35 cases this had to be repeated, but was ultimately successful; the total number of cases in which external version was ultimately successful was 258, and the reversion rate after this procedure was approximately 22 per cent. The reversion rate was reduced if external version was done after the thirty-third week of pregnancy. External version failed to turn the breech to a vertex in 77 cases; version subsequently occurred spontaneously in 28 of these cases; and in 13 cases the failure was subsequently overcome by the obstetrician; in 36 cases breech delivery was done. In 20 of the 36 cases of breech delivery the attitude was extension, and in one other case, semiextension. Very little liquor was estimated to be present in three cases, and there was one case of multiple pregnancy. The total number of breech deliveries was 85 in this series of 1,000 cases in which breech presentation was present at some time during pregnancy.

Breech presentation should be regarded as normal at a certain stage of pregnancy; spontaneous version usually occurs, although the reason for this requires further investigation. The findings in the cases of failed version indicate that an extended attitude and insufficient liquor are the chief causes of breech presentation at term, i.e., failure of spontaneous version, multiple pregnancy, and prematurity are also factors. External version is indicated as a therapeutic measure for breech presentation persisting after the thirty-second week of pregnancy.

HARVEY B. MATTHEWS.

### Puerperium

Rodriguez, Ximeno, M.: Spontaneous Expulsion of an Intraparietal Uterine Tumor During the Puerperium, *Arch. urug. de med. cir. y especialid.* 23: 349, 1945.

The author reports a case in which on the second postpartum day, a myoma the size of an eight months' baby's head was expelled spontaneously. During pregnancy a fibromyoma was suspected, because the author felt a mass in one side of the uterus which made the abdomen appear too large for the particular period of pregnancy. The uterine tumor was expelled by the action of the uterine contractions and the process of involution. In this case the puerperium was afebrile, the lochia were normal, and the uterus involuted well.

J. P. GREENHILL.

Palik, F., and Rechwitz, K.: The Cause of Late Bleeding in the Puerperium, *Monatschr. f. Geburtsh. u. Gynäk.* 117: 74, 1944.

In nine cases of delayed puerperal hemorrhage (four after full-term labor and five after abortions) the only cause found for the bleeding was hyaline degenerated decidua. The degeneration of the decidua probably began before delivery or abortion due to the activity of the trophoblast. The liquefaction and expulsion of the decidua was probably interrupted because the fibrinous degenerated decidua failed to set up a round cell demarcation as protection. Treatment consisted of instrumental removal of the decidual remnants. In abortion cases, the early onset of menstruation may bring about spontaneous healing.

J. P. GREENHILL.

Perez, M. L., and Blanchard, O.: Preventive Local Chemotherapy in Operative Obstetrics, *Obst. y ginec. latino-am.* 3: 161, 1945.

The authors again emphasize the great value of the prevention of puerperal sepsis following operative deliveries by forceps, version and extraction, manual removal of the placenta, etc. They instill 5 Gm. of sulfanilamide powder into the uterine cavity by means

- New Orleans Obstetrical and Gynecological Society.** (1924) *President*, E. L. Zander. *Secretary*, R. A. Grasser, 2700 Napoleon Ave., New Orleans, La. Meetings held every other month.
- St. Louis Gynecological Society.** (1924) *President*, Otto Krebs. *Secretary*, John E. Hobbs, 630 S. Kingshighway, St. Louis, Mo. Meetings second Thursday, October, December, February, and April.
- San Francisco Gynecological Society.** (1929) *President*, Albert M. Vollmer. *Secretary*, Daniel G. Morton, University of California Hospital, San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.
- Texas Association of Obstetricians and Gynecologists.** (1930) *President*, T. F. Bunkley. *Secretary*, J. McIver, 714 Medical Arts Bldg., Dallas, Tex.
- Michigan Society of Obstetricians and Gynecologists.** (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, Clarence E. Toshaeh. *Secretary*, John P. Ottaway, 1551 Woodward Ave., Detroit, Mich. Meetings first Tuesday of each month from October to May (inclusive).
- Central New York Association of Obstetricians and Gynecologists.** (1938) *President*, Raymond J. Picri. *Secretary*, Nathan N. Cohen, 713 E. Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.
- Alabama Association of Obstetricians and Gynecologists.** *President*, Gilbert F. Douglas. *Secretary*, Hunter Brown, 1922 South Tenth Ave., Birmingham, Ala.
- San Antonio Obstetric Society.** *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.
- Seattle Gynecological Society.** (1941) *President*, Gerhard Ahnquist. *Secretary*, Roger E. Stewart, Stimson Bldg., Seattle, Wash. Meetings held on third Wednesday of each month.
- Denver Obstetrical and Gynecological Society.** (1942) *Secretary*, Emmett A. Meehlcr, 1612 Tremont St., Denver, Colo.
- Wisconsin Society of Obstetrics and Gynecology.** (1940) *President*, Roland S. Cron. *Secretary*, Robert E. McDonald, 425 E. Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.
- San Diego Gynecological Society.** (1937) *President*, R. C. Hall. *Secretary*, D. Dalton Deeds, 2001 Fourth Ave., San Diego, Calif. Meetings held on the last Wednesday of each month.
- North Dakota Society of Obstetrics and Gynecology.** (1938) *President*, Ralph E. Leigh, Grand Forks. *Secretary*, G. Wilson Hunter, 807 Broadway, Fargo, N. D.
- Virginia Obstetrical and Gynecological Society.** (1936) *President*, S. E. Oglesby. *Secretary*, L. L. Shamburger, 628 State Office Bldg., Richmond 19, Va. Next meeting not announced.
- Columbus Obstetrical and Gynecological Society.** (1944) *President*, Wynne M. Silbernagel. *Secretary*, Zeph J. R. Hollenbeck, 9 Buttles Ave., Columbus, Ohio. Meetings held fourth Wednesday of each month.
- Nassau Obstetrical Society.** (1944) *President*, George B. Granger. *Secretary*, William S. C. Dolan, 2870 Northern Blvd., Manhasset, N. Y. Meetings, bimonthly from October to May.
- Bronx Gynecological and Obstetrical Society.** (1924) *President*, Harry Gordon. *Secretary-Treasurer*, J. Irving Kushner, 1840 Grand Concourse, New York, N. Y. Meetings, fourth Monday monthly from October to May.
- Washington State Obstetrical Society.** (1936) *President*, John H. Fiorino, Everett. *Secretary*, H. H. Skinner, Yakima. Meetings, first Saturday of April and October.
- Kansas City Obstetrical and Gynecological Society.** (1922) *President*, J. Milton Singleton. *Secretary*, Richard C. Helman. Meetings, third Thursdays, September, November, January, March, and May, University Club.
- Los Angeles Obstetrical and Gynecological Society.** (1914) *President*, George E. Judd. *Secretary*, Carl E. Krugmeier, 2200 West Third Street, Los Angeles, Calif.
- North Carolina Obstetrical and Gynecological Society.** (1932) *President*, Wallace B. Bradford. *Secretary*, Richard B. Dunn. Meetings semiannually.
- The Society of Obstetricians and Gynecologists of Canada.** (1944) *President*, William A. Scott. *Secretary*, James Goodwin, 516 Medical Arts Bldg., Toronto, 5. Meetings held annually, date of next meeting to be announced later.
- Akron Obstetrical and Gynecological Society.** (1946) *President*, H. H. Gibson. *Secretary*, Alven M. Weil, 1030 First Central Tower Bldg., Akron 5, Ohio.

# ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES\*

(*Appears in January, April, July, October*)

- American Gynecological Society. (1876) *President*, Norris Vaux, Philadelphia, Pa. *Secretary*, Norman Miller, Ann Arbor, Mich. Annual meeting to be announced.
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons. (1888) *President*, A. D. Campbell, Montreal, Quebec. *Secretary*, James R. Bloss, 418-11th Street, Huntington, W. Va. Annual meeting Hot Springs, Va., Sept. 4-6, 1947.
- Central Association of Obstetricians and Gynecologists. (1929) *President*, Earl C. Sage, Omaha, Neb. *Secretary-Treasurer*, John I. Brewer, Chicago, Ill. Annual meeting Louisville, Ky., Sept., 1947.
- South Atlantic Association of Obstetricians and Gynecologists. (1938) *President*, Robert A. Ross, Durham, S. C. *Secretary*, T. J. Williams, University, Va. Annual meeting at the General Oglethorpe Hotel, Savannah, Ga., Feb. 7-8, 1947.
- A. M. A. Section on Obstetrics and Gynecology. *Chairman*, Philip F. Williams, Philadelphia, Pa. *Secretary*, William Mengert, 2211 Oak Lawn Ave., Dallas, Tex. Annual meeting Atlantic City, June, 1947.
- New York Obstetrical Society. (1863) *President*, Harvey B. Matthews. *Secretary*, R. G. Douglas, 530 East 70th St., New York City. Second Tuesday, from October to May, Yale Club.
- Obstetrical Society of Philadelphia. (1868) *President*, F. Sidney Dunn. *Secretary*, James P. Lewis, 1930 Chestnut St., Philadelphia, Pa. First Thursday, from October to May.
- Chicago Gynecological Society. (1878) *President*, Ralph A. Reis. *Secretary*, Herbert E. Schmitz, 25 East Washington St., Chicago 2, Ill. Third Friday, from October to June, Hotel Knickerbocker.
- Brooklyn Gynecological Society. (1890) *President*, John J. Madden. *Secretary*, William T. Daily, 142 Joralemon St., Brooklyn, N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn, N. Y.
- Baltimore Obstetrical and Gynecological Society. (1929) *President*, Lawrence Wharton. *Secretary-Treasurer*, John W. Haws, 9 E. Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.
- Cincinnati Obstetrical Society. (1876) *President*, Carroll J. Fair. *Secretary*, Joseph G. Crotty, 136 West McMillan St., Cincinnati, Ohio. Third Thursday of each month.
- Louisville Obstetrical and Gynecological Society. *President*, Layman A. Gray. *Secretary*, E. P. Solomon, Hegburn Bldg., Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.
- Portland Society of Obstetrics and Gynecology. *President*, Charles Hunt. *Secretary-Treasurer*, Karl H. Martzloff, 808 Medical Dental Bldg., Portland, Ore. Last Wednesday of each month.
- Pittsburgh Obstetrical and Gynecological Society. (1934) *President*, Charles J. Barone. *Secretary*, Eugene A. Conti, 519 North Highland Ave., Pittsburgh 6, Pa. First Monday of October, December, February, April, and June.
- Obstetrical Society of Boston. (1861) *President*, George Van S. Smith. *Secretary*, Paul A. Younge, 101 Bay State Road, Boston, Mass. Third Tuesday, October to April, Harvard Club.
- New England Obstetrical and Gynecological Society. (1929) *President*, Arthur E. G. Edgelow, Springfield, Mass. *Recorder*, Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and December.
- Pacific Coast Obstetrical and Gynecological Society. (1931) *President*, Goodrich C. Schaffer. *Secretary-Treasurer*, William Benbow Thompson, 6253 Hollywood Blvd., Los Angeles, Calif.
- Washington Gynecological Society. (1933) *President*, James R. Costello. *Secretary*, Geo. J. Ellis, 1150 Connecticut Ave., N.W., Washington, D. C., Fourth Saturday, October to May.

\*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

May we say here that this series does not include many patients we feel certain have endometriosis, although we have no pathologic proof. These we have been able to control so far without resorting to surgery. Our problem is, then: Is it possible in endometriosis to preserve a normal functioning, asymptomatic pelvis?

### Technique and Operative Procedure

Fig. 1 is a cross section of a uterus and its adherent adnexa encountered in endometriosis. This familiar picture demonstrates the usual adhesive bed of ovarian heteroplasia. We have arbitrarily labeled ovarian lesions as "slight" when there is no appreciable enlargement, "moderate" where the ovary is about 5 to 6 cm. in diameter, and "advanced" where enlargement was beyond 7 to 8 centimeters.

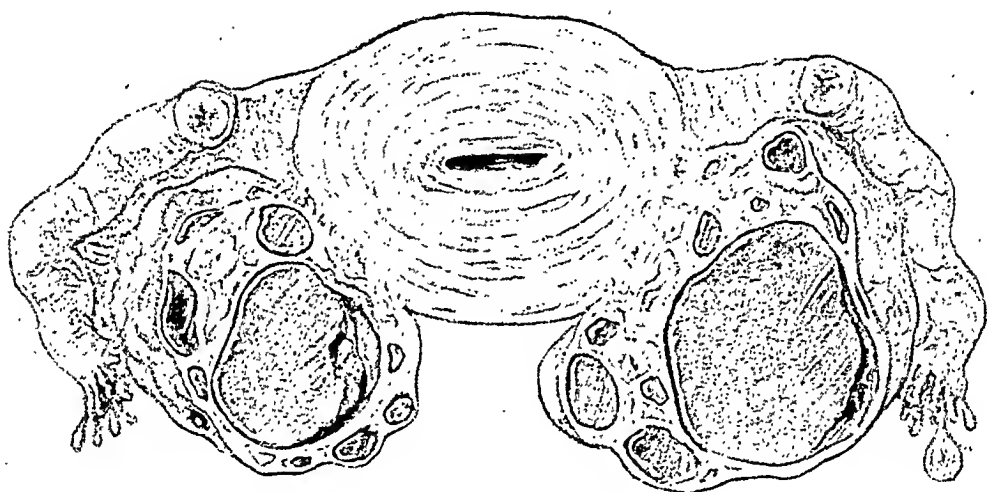


Fig. 1.

Fig. 2 illustrates our method of ovarian resection. The slight or early lesions were excised with repair of the ovary, usually by a small mattress suture of No. 00 chromic catgut on an atraumatic needle. Where we have moderate or advanced ovarian lesions, the ovary is delivered from its adhesive bed. Not infrequently rupture occurs during this procedure. The ovary is then opened by extending the point of rupture or, if no opening is present, by incision across the ovary directly opposite the hilus. The ovarian cyst is then opened like an oyster shell. All the affected tissue that can be seen is sharply dissected away and the ovary repaired with a continuous suture of No. 00 chromic catgut. Bleeding as a rule is not marked. However, if it does occur to any degree, small mattress sutures will control it.

In all cases, pathologic proof of diagnosis was obtained from resected or biopsied tissue. When removal of the uterus was deemed necessary, a pan-hysterectomy was done if the uterosacral ligaments and cul-de-sac involvement was not too marked. Appendectomies, if not previously done, were performed.

### Retrodisplaced Uteri

In our series of 80 cases we have noted a rather high incidence of retro-displacement (42.5 per cent). For this reason we have divided the cases into

# American Journal of Obstetrics and Gynecology

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## Original Communications

### CONSERVATIVE SURGERY IN ENDOMETRIOSIS\*

CLAYTON T. BEECHAM, B.S., M.D., PHILADELPHIA, PA.

*(From the Department of Obstetrics and Gynecology, Temple University Hospital and Medical School)*

CONSERVATIVE surgery in the treatment of endometriosis is the predilection of all gynecologists. That gynecologists vary somewhat on ideas of conservatism is to be expected. Dannreuther<sup>1</sup> feels that conservation of ovarian tissue in women over 35 years of age is of little importance, while Cashman<sup>2</sup> removes "the uterus and major lesions in the ovaries, if present," and attempts to "preserve all of the ovarian tissue possible." Graves<sup>3</sup> stated that removing ovaries hurts only neurotic women, yet he felt conservatism was in order when treating endometriosis. It finally becomes apparent that all gynecologists vary in their ideas of the importance of ovarian tissue, not to mention the child-bearing capacity in a normal, healthy, well-adjusted woman.

Novak<sup>4</sup> states that each case must be individualized as to the extent of the lesion and the age of the patient. To us, conservative gynecologic surgery means the removal of the least possible tissue to obtain the desired result. Hence, every attempt is made to preserve ovarian function to the age of 45 years or beyond if the lesion permits, and in previously sterile women the preservation of childbearing capacity to the age of 40 years. A patient with endometriosis who has her family obviously minimizes the latter consideration.

### Material and Problem

The material we offer consists of 80 consecutive cases encountered in the past six years. We have operated on 75 of these patients; we reoperated on four additional patients who had originally been operated upon elsewhere, and one patient operated upon elsewhere had recurring symptoms which we have been able to control without surgery.

\*Presented at a joint meeting of the New York, Philadelphia, and Boston Obstetrical Societies, held in New York City, April 9, 1946.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."



TABLE I. RETROVERSION AND ENDOMETRIOSIS

NO.	EXTENT AND LOCATION	AGE	SURGERY
1.	Advanced unilateral ovarian; utero-sacra; cul-de-sac	41	Supravaginal hysterectomy; unilateral salpingo-oophorectomy
2.	Advanced bilateral ovarian; utero-sacra; cul-de-sac	34	Supravaginal hysterectomy; unilateral salpingo-oophorectomy; resection one ovary
3.	Bilateral massive ovarian; cul-de-sac; uterosacra; chronic salpingitis	31	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
4.	Bilateral massive ovarian; chronic salpingitis adenomyosis	40	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
5.	Bilateral massive ovarian; utero-sacra; cul-de-sac	47	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
6.	Massive unilateral ovarian; adenocarcinoma of other ovary	56	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
7.	Adenomyosis with slight evidence of ovarian	56	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
8.	Advanced of all pelvic viscera	47	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
9.	Massive ovarian and cul-de-sac with myomas	48	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
10.	Massive ovarian; uterosacra and cul-de-sac with myomas	45	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
11.	Advanced of all pelvic viscera	37	Unable to remove more than the ovarian growth
12.	Bilateral advanced ovarian and sigmoid with myomas	47	Panhysterectomy; bilateral salpingo-oophorectomy
		44—	average age

TABLE II. (TWENTY-TWO CASES) RETROVERSION AND ENDOMETRIOSIS

NO. OF CASES	PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION
6	Uterosacral ligaments (slight)	30.3	Suspension
3	Unilateral slight ovarian, uterosacra	30.3	Suspension
2	Unilateral moderate ovarian, uterosacra	28.5	Suspension, resection one ovary
3	Bilateral slight ovarian, uterosacra	31.3	Suspension
1	Bilateral slight ovarian, uterosacra, sigmoid, appendix	33.0	Suspension
4	Bilateral moderate ovarian, uterosacra	30.75	Suspension, bilateral ovarian resection
2	One advanced ovarian, one moderate ovarian, uterosacra, broad ligament	35.0	Suspension, bilateral ovarian resection
1	Bilateral advanced ovarian; uterosacra, broad ligament	29.0	Suspension, bilateral ovarian resection
		31.0—	average age

Slight ovarian (endometriosis) means lesion on capsule without enlargement.

Moderate ovarian (endometriosis) means ovaries enlarged to about 5 to 6 cm.

Advanced ovarian (endometriosis) means ovaries enlarged to or beyond 7 to 8 cm.

menopausal symptoms fairly well controlled. In this group, all of the patients had one or more children with the exception of the 37-year-old woman who was unmarried.

It will be noted that only one patient had a complete hysterectomy. It was not feasible to do a panhysterectomy in the remaining eleven women because of marked uterosacral and cul-de-sac involvement.

The remaining 22 cases of retroversion and endometriosis are shown in Table II. The average age was 31 years. Nine women demonstrated early or minimal lesions, yet enough to fix the corpus uteri in the cul-de-sac as firmly as the most advanced case in the group.

two groups in order to note any difference in operative procedure. Further, if conservatism, by our definition, is possible, do the results justify the procedure?

The average age at operation of these 34 patients with endometriosis and retrodisplacement was 35.5 years. There were many pelvic complaints in this group; however, consultation was sought in the main because of varying grades of dysmenorrhea and dyspareunia with associated menorrhagia and/or metrorrhagia. One patient complained of backache, while two came to us for post-menopausal bleeding only.

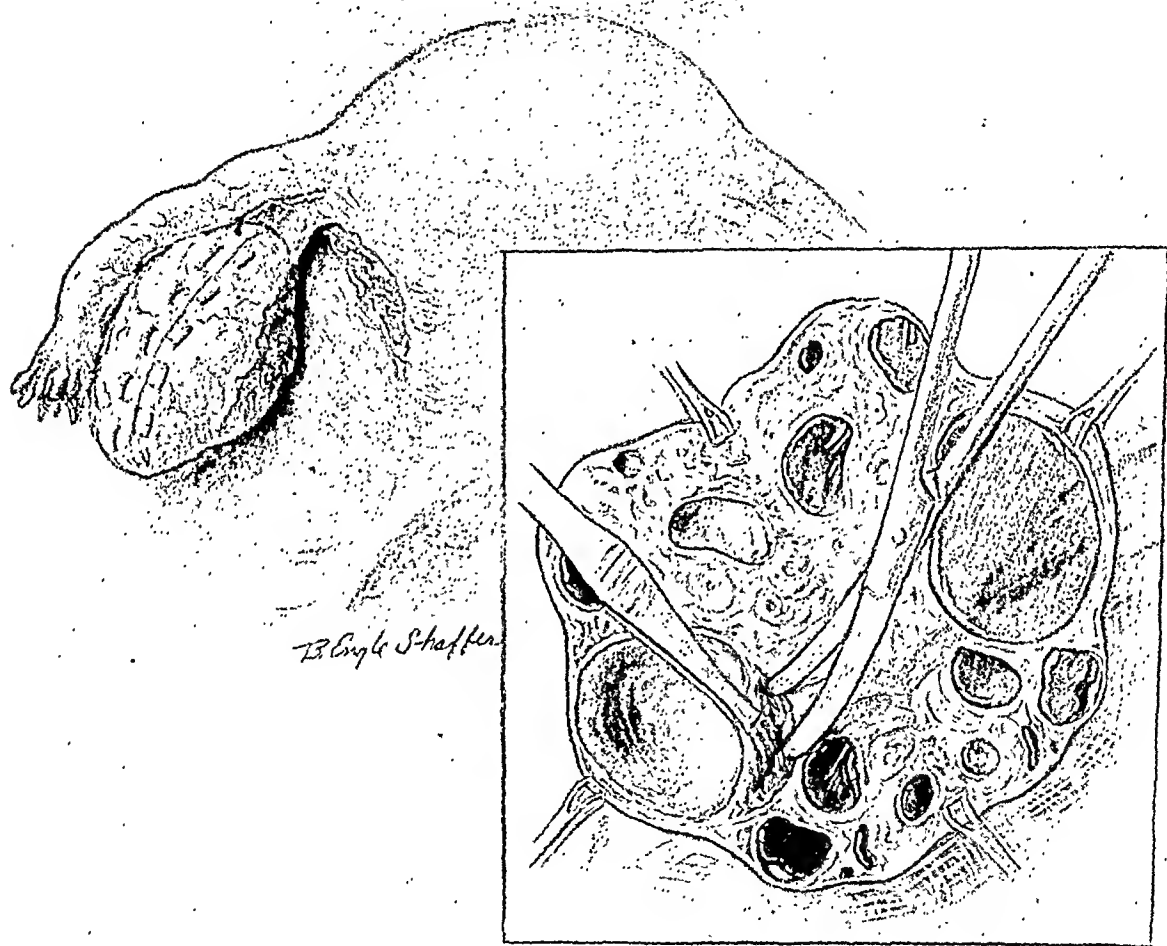


FIG. 2.

Table I (12 cases) summarizes the most severe cases in the retrodisplaced group. All of these patients had known retroversion for years. We consider the surgery to be radical in all. The ages ranged from 31 to 56 years, with an average age of 44 years. Unfortunately, three women were in the fourth decade of life, and in only one was any degree of conservatism possible, i.e., to leave ovarian tissue. A normal ovary was left in another patient 41 years of age. Both of these women are symptom free after three years, although endometriosis is palpable in the uterosacral ligaments at the moment. Two cases that were past the menopause at the time of operation (one with ovarian carcinoma) are free of symptoms and palpable pathology. The remaining eight have their

TABLE IV. UTERUS ANTERIOR—ENDOMETRIOSIS

NO.	PATHOLOGY AND EXTENT OF LESION	AGE	OPERATION
1.	Adenomyosis	44	Supravaginal hysterectomy
2.	Adenomyosis	42	Supravaginal hysterectomy
3.	Adenomyosis	40	Panhysterectomy
4.	Adenomyosis	30	Panhysterectomy
5.	Adenomyosis	40	Supravaginal hysterectomy
6.	Adenomyosis and myomas	45	Panhysterectomy
7.	Adenomyosis, myomas, broad ligament	43	Panhysterectomy
8.	Adenomyosis, unilateral moderate ovarian	49	Supravaginal hysterectomy, unilateral salpingo-oophorectomy
9.	Adenomyosis, advanced bilateral ovarian, uterosacrals, cul-de-sac	36	Supravaginal hysterectomy, unilateral salpingo-oophorectomy, resection one ovary
10.	Adenomyosis and complete prolapse	53	Vaginal hysterectomy
11.	Adenomyosis, myomas, cul-de-sac, unilateral advanced ovarian	49	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
12.	Adenomyosis, bilateral moderate ovarian	59	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
13.	Adenomyosis and myomas	51	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
14.	Adenomyosis, myomas, advanced ovarian, cul-de-sac	42	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
15.	Adenomyosis, myomas, bilateral advanced ovarian, cul-de-sac	40	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
		44—average age	

TABLE V. UTERUS ANTERIOR—ENDOMETRIOSIS

NO.	PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION
1.	Bleeding endometriosis in cul-de-sac with 5 weeks' pregnancy	27	Exploratory only
2.	Implants on bladder and round ligament	29	Presacral neurectomy
3.	Bilateral advanced ovarian	30	Resection both ovaries
4.	Bilateral advanced ovarian	38	Resection both ovaries
5.	Bilateral moderate ovarian, utero-sacrals	29	Resection both ovaries
6.	Bilateral advanced ovarian, unilateral chronic salpingitis	30	Unilateral salpingo-oophorectomy resection one ovary
7.	Unilateral moderate ovarian, utero-sacrals, broad ligament, sigmoid	38	Unilateral salpingo-oophorectomy
8.	Bilateral advanced and moderate ovarian, uterosacrals, cul-de-sac	34	Unilateral salpingo-oophorectomy resection one ovary
9.	Unilateral moderate ovarian	39	Unilateral salpingo-oophorectomy
10.	Bilateral advanced ovarian, cul-de-sac	41	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
11.	Bilateral advanced ovarian, cul-de-sac	46	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
12.	Bilateral advanced ovarian, cul-de-sac, chronic salpingitis	40	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
13.	Bilateral advanced ovarian, tubal, sigmoid, cul-de-sac	42	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
		36—average age	

ovarian tissue in situ in 46 per cent of the patients. None of these patients have pelvic complaints, although, again, endometriosis is palpable.

Table IV illustrates 15 cases of adenomyosis and adenomyosis with myomas and/or heteroplasia in the adnexa. The average age of this group was 44 years. All the operations must be considered radical in this group, although we were able to conserve all or part of the ovaries in 66 per cent of the patients. One patient was unmarried when we operated. the remainder of the group had two

Infertility concerned seven patients, and four of these have conceived (two delivered, one aborted at eight weeks, and one is pregnant now). The most advanced case in the group (certainly the most likely candidate for an operative failure) conceived four years after surgery. Only one patient continued to have the same complaints we had hoped to relieve with operation. Medication afforded no relief. However, she conceived eight months after suspension and resection of one ovary. Another patient, two and one-half years after operation, has a recurrence of dyspareunia with an increase in cul-de-sac growth. She refused to attempt pregnancy. All the patients that conceived had no endometriosis palpable after the sixteenth week of pregnancy.

It is of interest to note that the uterosacral ligaments were involved in 91.3 per cent of the patients, while 72.7 per cent demonstrated ovarian lesions. In all cases the Baldy-Webster technique was used. There have been no recurrences of retrodisplacement, in spite of clearly palpable endometriosis in most instances. Progress of the disease is watched for mainly in the uterosacral ligaments, and in one instance we have been able to detect spread into the cul-de-sac or surrounding broad ligaments.

### Uterus in Normal Position

There were 46 cases, or 57.5 per cent, of the series of 80 cases that had a normally placed uterus. We have divided these into groups of like pathology. Table III lists 13 cases of endometriosis with associated myoma uteri. It will be seen that the average age is 43 years, and again the need for conservatism was not great. In only one patient, aged 37 years, did we have the complaint of infertility along with the usual symptoms. This individual is now two years postoperative, has not conceived, but is symptom free. In all but this one case, the myomas precluded anything but hysterectomy. We were able to salvage

TABLE III. UTERUS ANTERIOR—ENDOMETRIOSIS AND MYOMATA

NO.	PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION
1.	Bilateral moderate ovarian, round ligament, myomas	37	Myomectomy, ovarian resection
2.	Myomas, slight bilateral ovarian	40	Supravaginal hysterectomy
3.	Myomas, omental endometriosis	38	Supravaginal hysterectomy, resection omentum
4.	Myomas, moderate unilateral ovarian	40	Panhysterectomy, unilateral salpingo-oophorectomy
5.	Myomas, unilateral moderate ovarian	41	Supravaginal hysterectomy, unilateral salpingo-oophorectomy
6.	Myomas, unilateral moderate ovarian and uterosacrals	36	Supravaginal hysterectomy, unilateral salpingo-oophorectomy
7.	Myomas, bilateral advanced ovarian, cul-de-sac	44	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
8.	Myomas, bilateral moderate ovarian, cul-de-sac	48	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
9.	Myomas, bilateral advanced ovarian	41	Panhysterectomy, bilateral salpingo-oophorectomy
10.	Myomas, bilateral slight ovarian	55	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
11.	Myomas, bilateral moderate ovarian, tubal, sigmoid	45	Panhysterectomy, bilateral salpingo-oophorectomy
12.	Myomas, bilateral moderate ovarian	44	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
13.	Myomas, bilateral slight ovarian, cul-de-sac	55	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
			43—average age

Since the remaining four patients had children, they created not too great a problem. They all had one constant feature in history, i.e., the pain they were originally operated upon for was in no way improved by the first operation. None of them was the least bit interested in further conservative surgery but requested that everything responsible for their pain be removed. One 45-year-old patient in this group needing reoperation we classed as a failure since she was never free of pain following the first operation.

### Comment

Nineteen patients, or 23.75 per cent, in the entire series were 45 years or older. Their treatment was radical although we salvaged ovaries in three instances. All of these patients have been well and we have no regrets at leaving the ovaries in three women over 45 years of age. Sixty-one, or 76.25 per cent, of the patients in the series were under 45 years of age. They constituted the main problem. Conservative surgery was impossible to any degree in 15 instances (24.5 per cent). Ovarian tissue was salvaged in whole or in part (by resection) in 14 patients (23 per cent). Childbearing capacity was retained in 32 cases (52.5 per cent). Follow-up examination revealed that for a period of one to six years all of these sixty-one cases have been free of complaints save two. One, at least, is temporarily asymptomatic with her pregnancy. A large share of the conservative treatment was possible through correction of a retrodisplaced uterus with its prolapsed adnexus.

We have been more than a little impressed with the incidence of retrodisplacement and endometriosis. It is well known that retrodisplacement receives scant attention in many quarters. This may be due to an overcorrection away from the days when it received entirely too much attention. Certainly an incidence of 42.5 per cent points to more than a casual relationship. Curtis<sup>5</sup> states, "In recent years we have learned that misplaced endometrial tissue is common with retrodisplacement." Sampson tells us in Sutton's<sup>6</sup> paper that, "The uterus is often but not necessarily always retrodisplaced." Watkins<sup>7</sup> injected contrast media into a retrodisplaced uterus without pressure and demonstrated it in the cul-de-sac. He points out the frequency of retrodisplacement and cul-de-sac endometriosis. However, the only figures we have found were those of Keene and Kimbrough,<sup>8</sup> finding an incidence of 13.5 per cent retrodisplacements while King<sup>9</sup> reports 21 per cent.

That there is a relationship in these two conditions cannot be denied. One wonders if the uterosacral ligaments may be a starting point in many of these cases since the minimal lesions were always there. Our feeling is that retrodisplacement with its mechanical interference with blood supply causing broad ligament varicosities, engorged cystic prolapsed ovaries, and passive congestion in the uterus, are accelerating factors in the metaplasia. For this reason we believe all women with retrodisplaced uteri should be observed at regular six-month intervals. Should they develop symptoms or demonstrate anything but a freely movable uterus a suspension is in order. In this way early lesions may be picked up while minimal, conservative surgery can be instituted and our salvage rate for the integrity of the internal pelvic viscera far higher. It would

or more children. The problem was one largely of trying to salvage ovarian tissue. Not considering four menopausal or postmenopausal patients, two women were surgically castrated between the ages of 40 and 42 years. In the latter two instances, conservatism seemed to us out of the question.

In Table V we have listed 11 cases of uncomplicated endometriosis, and two with additional findings. One interesting case was operated upon for ectopic pregnancy and was found to have bleeding endometrial tissue in the cul-de-sac (proved by biopsy). Another patient had minimal endometriosis of the bladder and round ligament with probable adenomyosis, in which case we locally excised the lesions and did a presacral neurectomy. Endometriosis was so extensive in 31 per cent of the patients (all 40 years old or over) that we could salvage no healthy ovarian tissue. It would seem in our attempt to group lesions according to extent that the treatment has varied greatly, i.e., ovarian resection in one advanced state and removal in another. Our explanation for this lies in the fact that one massive endometrial cyst when resected had some grossly healthy tissue, while another equally large growth seemed to lack even a small fragment of normal ovarian substance to be left behind.

Cases 3 through 8 could have had a complete ablation of the internal pelvic viscera according to usual standards of treatment. We are happy to note that these patients have none of their former complaints after a follow-up of one to six years. Thus far, in retrospect, we would not have changed the operative procedure in any of this group. Case 3 had a child 10 years of age when she was operated upon, and she was most desirous of another. She is symptom free so far, but has failed to conceive.

TABLE VI. FAILURES; OPERATED ELSEWHERE; FIVE CASES

PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION OR TREATMENT
Advanced sigmoid (partial obstruction), cul-de-sac (9 years from previous operation)	26	Supravaginal hysterectomy and remaining tube and ovary
Advanced ovarian, cul-de-sac (4 years from previous operation)	45	Supravaginal hysterectomy and remaining tube and ovary
Adenomyosis, advanced ovarian and cul-de-sac (6 years from previous operation)	34	Supravaginal hysterectomy and remaining tube and ovary
Adenomyosis, moderate ovarian (5 years from previous operation)	32	Supravaginal hysterectomy and remaining tube and ovary
Moderate ovarian, cul-de-sac (5 years from previous operation)	34	Observation and control of dysmenorrhea with benzedrine and aspirin

In Table VI are listed five failures. These women had been operated upon conservatively elsewhere at the intervals stated in the table. Case 1 had a tragic history. Originally at 17 years of age a large endometrial cyst ruptured and the affected ovary was removed. She had no symptoms until 24 years of age when dysmenorrhea occurred with increasing severity. The following year the patient married and used contraception. We were consulted after six months of married life. At this time the patient not only had severe dysmenorrhea but crampy, intermittent pain in the left lower quadrant. Establishing a diagnosis of endometriosis was not difficult. The patient was advised to conceive if possible in the hope of slowing up the endometrial process and further hoping to have a family before a second operation was necessary. The patient could not conceive. Partial bowel obstruction soon put in its appearance and we were forced to operate at 26 years of age. The rectosigmoid and cul-de-sac involvement was so advanced that we had no other course but to remove the remaining tube, ovary, and uterus. The psychic trauma to this individual was marked.

but in some instances the patient is a very unhappy person for the rest of her life. In our clinic at Temple University that has been the rule and it has been surprising to me the number of instances in which conservatism can be practiced in certain patients who appeared hopeless on examination of the pelvis, and in whom the results have been very gratifying.

One of the problems mentioned, which I think is rather questionable, is that endometriosis is the result of retroversion. Certainly, endometriosis that perhaps begins in the ovaries and the cul-de-sac and, as it proceeds, sets up an inflammatory reaction may in many cases be the cause of the retroversion.

DR. WILLIAM P. HEALY (New York).—I would have been tempted to be less conservative than the essayist under similar conditions. For example, I doubt if I would try to conserve ovarian function in a woman 45 years of age with bilateral endometriosis. I would feel that we could probably satisfactorily control any annoying symptoms which the patient might have from total hysterectomy and castration by medical measures.

I definitely agree with Dr. Beecham in the extreme importance of recognizing fixed retroversion caused by endometriosis. Therefore, in a young woman who has some dysmenorrhea and probably is sterile and may have some dyspareunia, I believe there is an indication for surgery, not because of the retroversion, but because of her symptoms and the endometriosis, which must be present.

Now, why is the uterus retroverted? Not so much because the uterosacral ligaments are invaded and infiltrated by the glandular deposits, but because the rectum or rectosigmoid creeps up on the back of the uterus and pulls the uterus down into the cul-de-sac.

DR. FRED A. SIMMONS (Boston).—I can only cite Dr. Meigs' observations at the Massachusetts General Hospital and am curious to know if Dr. Beecham has the same findings. We find that the incidence of endometriosis is definitely greater in the private than in the ward patients. This may possibly be due to the restraint of normal pregnancy in the private group as compared with the ward group, and possibly to late marriage in the private group due to educational hazards toward early marriage and consequent reduced fertility in that group. The incidence of endometriosis in Dr. Meigs' private patients is around 40 per cent, and the ward incidence is 5 per cent. He is always looking for it and finds it in the uterosacral ligaments usually. In the ward patients we find it more commonly, if it is looked for, than we did ten or fifteen years ago.

DR. ROBERT A. KIMBROUGH (Philadelphia).—Some years ago Dr. Floyd Keene and I reported a series of 108 cases, in 48 of whom one or both ovaries were conserved. Within a period of five years only three patients required subsequent treatment. Of those in whom the possibility of pregnancy was conserved, 28 per cent had subsequent normal pregnancies.

I believe there is no question that conservative surgery is indicated in endometriosis for three very specific reasons: first, endometriosis is not a malignant condition; it is possibly in some few cases clinically, but never in itself histologically, malignant; in any benign condition conservative surgery is indicated. That is a broad general statement, but I think most of us will subscribe to it. In the second place the existence and spread of endometriosis is absolutely dependent upon ovarian function. When we operate on a patient with endometriosis and leave ovarian function, we are perfectly aware of the possibility that the endometriosis may continue to spread, and the present amount of endometriosis will persist and may continue to cause symptoms. That is the possibility, but since endometriosis is dependent upon ovarian function, and since irradiation is a very simple method of controlling ovarian function, it seems that conservative measures are indicated in the treatment of this condition. The third reason which warrants the use of conservative measures is the fact that this lesion is extremely slow in its development and spread; those patients who may later require further therapy may, therefore, enjoy the advantages of continued ovarian function for several additional years.

DR. JAMES R. MILLER (Hartford).—We see a great deal of this condition and I, like the others, bemoan the fact that it occurs in young women.

seem thus far in this small series that when endometriosis and retrodisplacement are present suspension of the uterus retards the heteroplastic spread.

We believe resection of the ovaries in an attempt to uncover normal tissue is a worth-while procedure. Cattell and Swinton,<sup>10</sup> in a series of 43 cases, believe that complete ovarian involvement in endometriosis is not common and therefore emphasize conservatism. Failures in conservative surgery have been reported as high as 29 per cent by Pemberton<sup>11</sup> and as low as 7 per cent by Crile.<sup>12</sup> In the 46 cases under 45 years of age in which we saved the uterus, tubes, and ovaries or ovaries alone, we failed in one case to relieve pain, yet the patient conceived. In one other recurrent symptoms appeared at two and one-half years.

An assessment of operative success or failure can be made at the follow-up examination. As we have noted above, the outstanding feature of the failure of conservative surgery was unremitting pain.

### Conclusions

1. There seems to be a close relationship between retrodisplacement and endometriosis.

2. The nonpathologic retrodisplaced uterus should be observed at regular intervals for signs of fixation indicating a surgical need for treatment of probable endometriosis.

3. We have found it possible to salvage ovarian tissue in situ in 23 per cent of women under 45 years of age.

4. Childbearing capacity was salvaged in an additional 52.5 per cent of women under 45 years of age.

5. For many years the diagnosis of endometriosis has been a *carte blanche* to surgeons for castration.

6. We feel that conservative surgery is definitely worth while and should be the major consideration when operating upon endometriosis.

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### Discussion

DR. JOHN MONTGOMERY (Philadelphia).—I believe that we are all in accord with the fundamental principles enunciated in trying to be conservative in young women in the childbearing years with the extensive endometriosis which requires complete removal of the ovaries and uterus. It is easy enough to take out the uterus and, as a rule, we cure the patient,



By allowing one ovary to remain it would stimulate further activity and cause trouble from the endometrial implants, including bleeding into the peritoneal cavity.

DR. BEECHAM (Closing).—Dr. Montgomery stated that he believes endometriosis causes retrodisplacement. Six cases in our series presented minimal lesions on the left uterosaeral ligament; these were so small it seems hard to believe that the endometriosis was an etiologic factor in the retrodisplacement.

In reply to Dr. Healy, we left ovaries in women 45 years of age and over only if they were normal grossly and the pathology was limited to the uterus. Both Dr. Miller and Dr. Healy mentioned the use of x-ray in the therapy of endometriosis. We have used it only for castration purposes, since it is very difficult to measure a subcastration dose in any given individual. We have seen permanent amenorrhea result from the so-called stimulating dose of x-ray to the ovaries for secondary amenorrhea and other endoeropathies.

Dr. Simmons mentioned Dr. Meigs' work in reference to the frequency of endometriosis in private practice. The cases in this paper were all private patients, the disease having been seen but rarely in the wards at Temple University and Philadelphia General Hospitals. Meigs holds the view that late marriage and prolonged uninterrupted menses in any woman favors the development of endometriosis. This undoubtedly is one of the chief causes for the high incidence in private patients.

Dr. Kimbrough's series of cases have yielded a higher per cent of pregnancies in sterility patients than any other report we have seen. Dr. Kimbrough brought up a perplexing question; namely, that endometriosis depends on "ovarian function" for continual growth and development. In this we are all agreed, yet the ovaries function in pregnancy. In fact, the estrogen curve goes up as term approaches and endometriosis regresses to nonpalpable lesions.

Dr. Studdiford asked what kind of an ovarian carcinoma was encountered with endometriosis. It was an adenocarcinoma. Our impression was that the patient had bilateral endometrial cysts and one had undergone malignant change.

Dr. Frost has been able to demonstrate ovulation by endometrial biopsy after ovarian resection in cases of endometriosis. We have followed a number of the same type patients with daily rectal temperature readings for a short time following operation and have found all to have anovulatory bleeding for several months.

Our findings have been similar to Dr. Davies', that the left uterosaeral ligament is the usual starting point for endometriosis.

Dr. Bunzel asked about bleeding of heteroplastic tissue in the free abdominal cavity. We have found it in the one reported case in the cul-de-sac, associated with early pregnancy.

I think there are some other conservative measures that may be brought to bear. Occasionally, we encounter endometriosis in the rectovaginal septum and then it causes more alarm than it does when it is higher up. I think that direct x-ray, and even radium seeds applied locally, will control the lesion.

I would also like to mention the use of testosterone propionate or methyl testosterone by mouth as one of the conservative measures which may be tried. It is quite striking to see the reduction in size of the endometriotic lesions which will occur under testosterone propionate. That, of course, cannot be pushed too far, and caution must be used to keep the dosage well below 200 mg. per mouth.

DR. WILLIAM STUDDIFORD (New York).—I would like to ask Dr. Beecham the nature of the carcinoma that he found in association with endometriosis in the opposite ovary. The reason I ask that question is that we have now five cases in which there is a very strong indication that the ovarian carcinoma is actually adenocarcinoma arising on the basis of endometritic deposits in the ovary. In one of the cases the likelihood is almost beyond question.

I do not believe you can regard endometriosis in elderly women as something which is entirely beyond the pale of malignancy.

DR. INGLIS F. FROST (New York).—In the last two years I have been trying to see how much ovarian tissue could be resected and still maintain a positive secretory phase in the endometrial biopsy. We have had 25 cases at the Woman's Hospital in which we resected ovaries, leaving ovarian tissue not much larger than the head of a pin. When the secretory phase of the endometrium is maintained and the patients are ovulating they generally become pregnant easily, but it is very difficult for them to retain the pregnancy, and we feel that they must be given a great deal of supportive treatment in the way of progesterone.

DR. JOSHUA W. DAVIES (New York).—I feel that this is not a surgical condition, but that it is due to some endocrine dysfunction which results in the production of a great deal of pain in the pelvis, rendering it essential that we relieve patients so afflicted. Relief may be afforded by severing the adhesions in the pelvis, and thus holding the uterus anteriorly. I do not approve of removing the uterus or adnexa in these patients.

Dr. Beecham said that the uterosacral ligament is involved in many of these cases, chiefly on the left side. The uterosacral ligament is not a ligament alone; it is a very dense structure containing lymphatics, and when there is an inflammatory condition of the lymphatics there is production of scar tissue. If the uterus is involved with endometriosis, the denser peritoneum over the uterus is carried out to the lymphatics in the uterosacral ligament which run to and up the rectum. It is scar tissue in the uterosacral structure on the left side which draws the uterus against the cervix and rotates the uterus to the opposite side of the sacrum, to which the sigmoid is attached; this causes congestion in the pelvic circulation. Thus the uterus becomes fixed and the veins distended. If we fail to relieve these patients of their pain I believe surgery should be resorted to and in operating for retroversion, if it is possible to separate the sigmoid from the cervix and hold the uterus anteriorly, these patients may be temporarily relieved.

DR. E. EVERETT BUNZEL (New York).—There is one phase of the subject which was not touched upon and which was brought to my attention by a recent case. The patient was 40 years old with an ovarian mass on the right side and gave a history of having had a profuse, painful, long period. I opened the abdomen following a curettage, and found free blood in the abdominal cavity. Some of the blood was bright, while some had the character of the chocolate material found in Sampson's cysts. The cyst on the right side was not ruptured, but was adherent. After wiping away the blood in the pelvis we found several endometrial implants on the posterior aspect of the uterus, the posterior aspect of the broad ligament, and in the cul-de-sac. I wonder whether these implants are prone to bleed into the peritoneal cavity. At 40 years of age I did not take a conservative attitude, but removed the uterus and cervix together with the adnexa on both sides. The patient was married, but had never conceived.

longed labor on the fetus), "prolonged labor per se exerts a deleterious effect on both the maternal and fetal organisms and the severity of this deleterious effect increased progressively with the duration of labor."

During the clinical course of these patients with prolonged labor, there may arrive a time when one must resort to an active policy. Manual dilatation of the cervix, the dilating bag, Dührssens' incisions, difficult forceps operations, and radical cesarean section have been recommended in the past. Certain of these methods are obsolete. All such methods are bound to carry an appreciable increase in the maternal and fetal mortality and morbidity rate.

The employment of x-ray pelvimetry does contribute a certain sense of security in the proper conduct of labor in these cases which are experiencing ineffectual labor. However, this can be deceptive if we should take the attitude that all patients who present little or no evidence of cephalopelvic disproportion will have their babies by the pelvic route if given a sufficient length of time to complete their labors. The obstetrician with this attitude must accept some increase in the infant stillbirth and neonatal death rate in proportion to the number of added hours or days of labor which are allowed to transpire. This group becomes even more important because we are concerned with good babies, at least at the onset of labor. So often this is not true in other complicated obstetrical conditions.

It follows, therefore, that in realizing the increased infant stillbirth and neonatal death rate which accompanies prolonged labor, we should employ every means at our command to decrease the number of such cases. Until we know the cause or causes of the onset of labor, any attempt to treat successfully such patients can be done only empirically, and is, therefore, subject to a certain percentage of failures.

During the past five years at the Boston Lying-in Hospital, we have used posterior pituitary extract routinely on all patients who revealed any evidence of inertia during the course of any patient's labor. It was felt that this was the most reasonable policy if we were to obtain a true picture of the merits and demerits of this drug. Although the drug had been used in this clinic in previous years for the treatment of uterine inertia, its routine use was not carried out in all cases of inertia. It was felt that enough experience had been gained in the use of x-ray pelvimetry (Thom's method) to insure against the giving of the drug to any patient with definite cephalopelvic disproportion. In addition, experience had been gained with the different types of extraperitoneal cesarean sections which could be resorted to if any untoward results occurred from the use of the drug or if it failed to completely dilate the cervix.

The object in using the drug was as follows:

1. To attempt to decrease the number of cases of prolonged labor, by completing the dilatation of the cervix within the limits of the number of hours commonly associated with normal labor (thirteen to eighteen hours).

2. To treat cases of so-called prolonged labor with this drug in order to reduce the number of hours of the first and second stages of labor with its adverse effect on the fetus.

## THE TREATMENT OF PROLONGED LABOR WITH POSTERIOR PITUITARY EXTRACT\*

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**D**URING the past fifteen years, with the advent of accurate methods of x-ray pelvimetry, a better understanding of the mechanism of labor has been observed in both the normal and abnormal obstetric pelvis. Accurate measurement and accurate classification of the abnormal obstetric pelvis has contributed much to a more intelligent conduct of labor.

The trend in obstetrics during the latter years has been to emphasize the architecture of the bony pelvis as the major factor in the prognosis of a given labor, with less regard being given to the other factors involved. This attitude is understandable when we consider how little is accurately known regarding the cause of the onset or the continuation of effective uterine contractions.

Helpful as these different techniques of x-ray mensuration may be in evaluating the pelvic architecture, we are always faced with the problem of the type of labor a given case may experience. It is this unknown factor which makes every obstetric case at least a potential problem. Certainly, it is a common experience to observe the successful completion of labor, even in the presence of rather marked pelvic contracture where labor is accompanied by effective uterine contractions. For contrast, severe degrees of prolonged labor may occur only in the presence of soft-tissue dystocia when associated with the ineffectual powers of labor.

In the dystocia group which results from pelvic contracture, the proper treatment can usually be ascertained after a few hours of a trial test of labor. Exceptions do, of course, occur in a small percentage of so-called "borderline cases." However, in the treatment of the dystocia group resulting primarily from ineffectual labor, the correct procedure to obtain a good result is often difficult to determine.

In the absence of any evidence of cephalopelvic disproportion, the common terms which have been used to describe this latter group are atoni uteri (primary or secondary), cervical dystocia, and delayed or prolonged labor. No term is entirely satisfactory. In any event, whatever term one desires to use in describing such cases, the problem remains the same; namely, the inability of the cervix to become completely dilated.

Unfortunately, watchful expectancy is not always associated with brilliant results in these cases of prolonged labor resulting from uterine inertia. It is common experience that fetal damage and maternal complications may produce disasters of as great a magnitude in these cases as in those patients who are subjected to prolonged tests of labor in the presence of cephalopelvic disproportion. As Douglas and Stande<sup>1</sup> have so aptly stated (in studying the effect of pro-

\*Read before the Boston Obstetrical Society, November, 1945.

cervix. Desultory uterine contractions which might be continual for hours or even days were present in many of these patients in both groups, but if the above changes on the cervix could not be ascertained, the patient was considered to be in false labor and was so treated.

### Results

In Table I is recorded the age of the patients. The general age group follows a general trend both in the private and clinic series. Most of the cases were primiparous women; two-thirds were under 30 years of age.

TABLE I. AGE

	20 TO 29 YEARS	30 TO 39 YEARS	40 YEARS	TOTAL CASES
Private series, uncomplicated	442 61.2%	265 26.9%	10 1.50%	717
Boston Lying-in series, uncomplicated	460 72.5%	161 25.3%	15 2.30%	636
Private series, complicated	34 68.0%	16 32.0%	—	50
Boston Lying-in series, complicated	168 81.6%	36 17.5%	2 0.97%	206
Total cases	1,104	478	27	1,609

*Parity.*—In Table II it is shown that age and parity go hand in hand. About two-thirds of the entire series are primiparous women. There is one difference, however, to be observed between the private and the clinic series. There are many more primiparous patients treated in the clinic series than in the private series.

TABLE II. PARITY

	i-	ii TO iii	iv	TOTAL CASES
Private series, uncomplicated	390 54.4%	294 41.00%	33 4.50%	717
Boston Lying-in series, uncomplicated	452 71.0%	143 22.50%	41 6.40%	636
Private series, prolonged labor	44 88.0%	6 12.00%	—	50
Boston Lying-in series, prolonged labor	199 96.6%	2 0.97%	5 2.43%	206
Total cases	1,085	445	79	1,609

In Table III is recorded the parity of the complicated group occurring in the clinic series. It can readily be seen that there were very few multiparous women who came to so-called prolonged labor. These exceptions can be readily explained. This is a small but important number of patients who will compose a group who may be justifiably classified as "dangerous multiparas." These cases composed about 3 per cent of this complicated clinic group. This group deserves further comment. Suffice it to say that large babies, accompanied by some degree of pelvic contracture, were present in these multiparous patients and uterine inertia was of secondary importance.

The station of the head at the onset of labor is listed in Table IV. Only about one-fifth of the patients entered labor with the presenting part unengaged. It could not be established whether the patient who started in labor with an unengaged head was more likely to present evidence of prolonged labor. The station of the head at the onset of labor was not a factor in the production of prolonged labor.

3. It was hoped that the necessity for difficult pelvic operations, such as midforceps with or without Dührsens' incisions, could be brought to a minimum in these cases of prolonged labor.

These are desirable aims if these conditions could be fulfilled without increasing the stillbirth and neonatal death rate, or producing latent cerebral damage to the infant or any deleterious effect on the mother. For it has been suggested that prolonged labor, per se, was not necessarily harmful in itself, but prolonged labor accompanied by a difficult forceps operation was a combination that was extremely lethal to the baby.

It was felt that the drug must be used in a sufficient number of patients in order to evaluate it properly. Such evaluation should include (in addition to the objective stated above):

1. What are the limitations of the drug.
2. What type of case was most likely to result in failure when the drug had been used. The factors which might have contributed to such failure should be ascertained.
3. If the drug had any merit, would it be possible to evolve a rational method whereby the drug could be safely placed into the armamentarium of the treatment of cases of so-called prolonged labor resulting from uterine inertia.

### Material

This communication is concerned with reporting on 1,609 patients who had been given posterior pituitary extract during the first and second stages of their labors. These patients are divided into two series, 767 cases collected from private patients, and 842 cases from the clinic of the Boston Lying-in Hospital. The latter group is composed of cases treated during the past five years, while some of the records of the patients in the private series date back several years before x-ray pelvimetry and extraperitoneal cesarean section had become common obstetric techniques. This accounts for some of the differences in the private series in contrast to the clinic series, as for example, the type of operations necessary to complete delivery in each series.

Each of these series has been divided into two subgroups, the uncomplicated and the complicated. The element of time, i.e., the hours of labor which ensued, is the factor upon which these groups were classified. The number of hours of labor which must pass in order to make a diagnosis of prolonged labor varies in different clinics. We chose twenty hours of labor as the dividing line between the uncomplicated group and the complicated group. The diagnosis of prolonged labor was attached to the latter group. We realize that this is an arbitrary division. However, the normal length of primiparous labor is accepted as averaging from thirteen to eighteen hours. We extended the time to twenty hours in order not to include any cases in the prolonged labor group (complicated) who were not actually troublesome cases.

Many of the cases in both the complicated and the uncomplicated groups were diagnosed as patients with prolonged labor. Individual perusal of the patient's records did not substantiate such a diagnosis in many of the cases. Although the patients were experiencing at times irregular and painful contractions, the patient was not in true labor. For this report, the onset of true labor was defined and so recorded as beginning only when the uterine contractions were of such quality that definite changes could be recorded regarding either effacement, but more particularly still, some degree of dilatation of the

series had a first stage labor of forty hours or longer. It should be emphasized, however, that many of these patients were in so-called desultory labor for perhaps as long as twenty-four to seventy-two hours before the actual true labor began. During that time no change was noted in the cervix, and consequently the patient was not considered to be in labor. Consideration of this factor may account in part for the low incidence of prolonged labor in this series in contrast to the experience of other clinics.

The length of the second stage of labor in the uncomplicated group (Table VII) revealed a sharp contrast between the private and the clinic series. The clinic series was subjected to many more hours of second stage labor. The reasons for this marked difference could be explained by the following factors: (1) The individual attention which would be given to the private patient where the responsibility is dependent upon one person would necessarily make its effect felt in shortening the second stage of labor. (2) The increased amount of pituitary extract which was used in the private series would necessarily shorten the second stage of labor. (Tables X and XI). (3) In the clinic series a longer second stage of labor was believed justified in the hope that the patient would come to an easy low forceps operation. The drug was given specifically to further the descent of the fetal head in an attempt to reduce the need for a midforceps delivery. This would appear to be reasonable when we consider that the fetal mortality in the two series was approximately equal.

From the evidence presented here, we do not need to fear a prolonged second stage labor as long as the patient is making progress. The only fear in a prolonged second stage labor appears to be when progress has ceased. This is particularly true when this arrest of progress occurs with the presenting part on the perineal floor. It is generally agreed that if progress has ceased when this has occurred, delivery should be carried out with dispatch. To emphasize this, the babies that were lost in the clinic series (uncomplicated group, Table XV) occurred in a prolonged second stage labor associated with just such an arrest.

TABLE VII. LENGTH OF SECOND STAGE OF LABOR, UNCOMPLICATED GROUP

	1 HOUR	2 HOURS	3 TO 4 HOURS	5 TO 6 HOURS	7 HOURS	TOTAL
Private series	688 96.0%	29 4.0%	—	—	—	717
Boston Lying-in Hospital series	225 35.4%	173 27.2%	197 31.0%	32 5.0%	9 1.4%	636
Total cases	913	202	197	32	9	1,353

TABLE VIII. LENGTH OF SECOND STAGE OF LABOR, COMPLICATED GROUP

	1 HOUR	2 HOURS	3 TO 4 HOURS	5 TO 6 HOURS	7 HOURS	TOTAL
Private series	47 94.0%	3 6.0%	—	—	—	50
Boston Lying-in series	31 18.1%	76 44.7%	38 22.7%	19 11.1%	6 3.5%	170*
Total cases	78	79	38	19	6	220

\*Certain patients who were given pituitrin eventually had to be delivered by extraperitoneal sections or Dührssen's incision; hence, no second stage of labor.

In Table VIII is given the length of the second stage of labor in the complicated group. Again it will be seen that the clinic series was subjected to a much longer second stage labor, no doubt for reasons already mentioned.

In Table IX is listed the types of deliveries. It will be noted that there is a much higher incidence of midforceps operations in the private series. This

TABLE III. BOSTON LYING-IN HOSPITAL (CLINIC SERIES, COMPLICATED)

Parity:	i	ii to iii	iv
Cases:	199	*2	*5
Per Cent:	96.60	0.97	2.43

- \* (1) Para iv, large baby (8 lb., 10 oz.). Platypelloid pelvis.  
 (2) Para xiii, large baby (9 lb., 9 oz.). Platypelloid pelvis.  
 (3) Para iv, large baby (9 lb.). Platypelloid pelvis with android fore-pelvis.  
 (4) Para v, large baby (10 lb., 1 oz.). Gynecoid pelvis with android tendency.  
 (5) Para ii, large baby (9 lb., 1 oz.). Breech.  
 (6) Para iv, plastic operation between pregnancies.  
 (7) Para ii, no cause for dystocia.

TABLE IV. STATION OF HEAD AT ONSET OF LABOR

	HIGH	MID	LOW	TOTAL
Private series, uncomplicated	149 20.9%	251 35.0%	317 44.70%	717
Boston Lying-in series, uncomplicated	148 23.3%	393 62.0%	95 14.80%	636
Private series, complicated	14 28.0%	26 52.0%	10 20.00%	50
Boston Lying-in series, complicated	76 37.9%	128 61.4%	2 0.97%	206
Total cases	387	798	424	1,609

TABLE V. LENGTH OF FIRST STAGE OF LABOR

	4 TO 8 HOURS	9 TO 12 HOURS	13 TO 16 HOURS	17 TO 20 HOURS	TOTAL
Private series	409 57.0%	185 25.8%	78 10.9%	45 6.3%	717
Boston Lying-in Hospital series	388 61.0%	173 27.2%	74 11.6%	1	636
Total cases	797	358	152	46	1,353

In Table V the length of the first stage of labor is shown in the uncomplicated group in both series. Five-sixths of the patients had a first stage of labor of less than twelve hours, while half the patients delivered in less than eight hours. An overall average of the first stage of labor would fall between six and eight hours, which is about the average for a multiparous labor. With a high percentage of the primiparous women in the series, the overall length of the first stage of labor was, therefore, decidedly shorter than the usual standard taken for the average length of labor in primiparous patients. How many of these patients would have experienced prolonged labor if pituitary extract had not be given is problematical.

TABLE VI. LENGTH OF FIRST STAGE OF LABOR, COMPLICATED GROUP

	20 TO 29 HOURS	30 TO 39 HOURS	40 TO 49 HOURS	50 HOURS	TOTAL
Private series	44 88.0%	4 8.0%	2 4.0%	—	50
Boston Lying-in series	128 61.6%	54 27.2%	15 7.3%	9 3.9%	206
Total cases	172	58	17	9	256

In Table VI is shown the length of the first stage of labor in cases of prolonged labor. In the complicated group, nearly 90 per cent of the cases, the completed first stage of labor was short of thirty hours' duration. The labors were somewhat more prolonged in the clinic patients, but only 11 per cent of this



TABLE X. PITUITRIN, MAXIMUM DOSE

MINIMS	I	II	III	IV	V	TOTAL CASES
Private series, uncomplicated	213 29.8%	243 33.9%	145 20.2%	42 5.8%	74 10.3%	717
Boston Lying-in Hospital series, uncomplicated	592 93.1%	42 6.6%	2 —	— —	— —	636
Private series, complicated	9 18%	24 48%	10 20%	2 4%	5 10%	50
Boston Lying-in Hospital series, complicated	139 67.4%	45 21.9%	19 9.2%	3 1.5%	—	206
Total cases	953	354	176	47	79	1,609

TABLE XI. PITUITRIN, TOTAL DOSAGE

MINIMS	1 TO 4	5 TO 9	10 TO 14	15	TOTAL CASES
Private series, uncomplicated	475 66.3%	173 24.1%	43 6.0%	26 3.6%	717
Boston Lying-in Hospital series, uncomplicated	605 95.1%	28 4.4%	3 0.5%	—	636
Private series, complicated	30 60%	12 24%	7 14%	1 2%	50
Boston Lying-in Hospital series, complicated	116 56.3%	56 27.2%	19 9.2%	15 7.3%	206
Total cases	1226	269	72	42	1,609

series. This suggests that in the use of this drug the dosage should be increased until the patient has effective uterine contractions. We are justified in suggesting this when we consider the end results in the two series. It seems probable that our results in the clinic series (complicated group) might have been improved had we used the drug in increasing doses until a definite therapeutic effect was demonstrated.

Table XI reveals the total amount of drug used in a given labor. Again it will be seen that the total dosage used in the private series was much greater in most instances than in the clinic series. This again suggests the possibility that the drug could have been used in larger doses in order to obtain the most effective physiologic result.

TABLE XII. DEGREE OF CERVICAL DILATATION WHEN PITUITRIN WAS FIRST GIVEN

DILATATION	$\frac{1}{4}$	$\frac{1}{2}$	$\frac{3}{4}$	FULLY DILATED	TOTAL CASES
Private series, uncomplicated	58 8.1%	441 61.5%	46 6.4%	172 23.7%	717
Boston Lying-in Hospital series, uncomplicated	38 5.97%	32 5.03%	70 11%	496 78%	636
Private series, complicated	3 6.0%	38 76.0%	—	9 18%	50
Boston Lying-in Hospital series, complicated	2 0.97%	27 13.10%	72 34.95%	105 50.98%	206
Total cases	101	538	188	782	1,609

Table XII reveals the degree of cervical dilatation existing at the time that pituitrin was first administered during the first stage of labor. Here again it is seen that the drug was administered in the private series much earlier in labor than in the clinic patients. This may indicate that as soon as progress in labor

TABLE IX. TYPE OF DELIVERY

	NOR- MAL	LOW FOR- CEPS	MID- FOR- CEPS	HIGH FOR- CEPS	VER- SION	CRANI- OTOMY	BREECH	CESA- REAN	TWINS	TOTAL
Private series, uncomplicated	384 52.9%	277 38.1%	23 3.1%	9 1.2%	11 1.5%	—	18 2.5%	4 2.5%	-9 1.2%	726
Boston Lying- in series, uncomplicated	204 32.1%	421 66.2%	6 1.0%	—	3 0.5%	—	5 1.0%	—	-3 0.5%	639
Private series, complicated	12 23.5%	25 49.0%	7 13.9%	2 3.9%	3 5.9%	—	2 3.9%	—	-1 0.5%	51
Boston Lying- in series, complicated	18 8.6%	138 66.0%	16 7.65%	—	1 0.5%	2 0.95%	7 3.35%	27* 12.9%	-3 1.5%	209
Total cases	618	861	52	11	18	2	32	31	-16	1,625

\*Extraperitoneal (Waters) or exclusion type (Smith).

is offset, however, by an extremely low incidence of cesarean section. In contrast to this, there were no high forceps operations in the clinic series, while the midforceps incidence was very low. However, there were twenty-seven cases of extraperitoneal or exclusion types of cesarean section which gave a much higher incidence of cesarean section in the clinic series than in the private series. These differences can be readily explained when we consider that many of the private patients were delivered before the advent of extraperitoneal cesarean section or the general use of x-ray pelvimetry. It was considered advisable to do the occasional high forceps delivery where labor was prolonged and associated with possible intrauterine infection rather than subject the patient to a Porro cesarean section, which was then in order during the particular years in which many of these patients were delivered.

The use of the extraperitoneal or peritoneal exclusion cesarean section is a necessary method of delivery in certain cases of prolonged labor. It is a general policy of the clinic to use the extraperitoneal type where cesarean section is necessary for infected cases, or even in supposedly clean cases if labor is prolonged beyond twelve hours after the onset. This is particularly true if the fetal membranes have been ruptured prior to the beginning of labor.

There were 55 such operations performed in the past five years in the clinic of the Boston Lying-in Hospital. Four-fifths were of the Waters type and the remainder were the Smith exclusion type. There were two maternal deaths. One was due to shock and hemorrhage, and the other was an anesthetic death. There were two fetal deaths. It was interesting to note that these two fetal deaths (both due to asphyxia), occurred in babies whose mothers were allowed to continue in labor when progress had ceased for over twelve hours prior to section.

The indications for section could be divided roughly into thirds; namely, borderline cephalopelvic disproportion, questionable cephalopelvic disproportion with cervical dystocia, and finally, cervical dystocia per se. Uterine inertia was common to all, and it was felt in all of these patients that if labor was of good character, pelvic delivery was possible. Conservative obstetrics demand adequate tests of labor in these patients. Twenty-seven of these patients experienced prolonged labors. They were given posterior pituitary extract with poor effect during their labors in the hopes of overcoming the uterine inertia and associated cervical dystocia.

In Table X is detailed the maximum dose of posterior pituitary extract which was administered at any one time. Considerable differences in the dosage exists between the private and clinic series. It will be seen that much larger single doses of the drug were used in the private series in contrast to the clinic

who come to the hospital at full term with no complications, either obstetric or medical, in which the baby was normally developed and living at the onset of labor. Furthermore, the course of the mothers during labor was entirely normal in respect to both character and length of labor. The mothers were delivered either normally or by outlet forceps. No pituitary extract was given to any of these patients during the first and second stages of their labor. For unascertainable reasons, the baby died in utero during labor or in the neonatal period. As is shown in the chart, comparatively few died from intracranial hemorrhage; the majority died of intrauterine asphyxia. During this five-year period, there were 39 such cases associated with 11,507 normal or outlet forceps deliveries, giving a total percentage mortality of 0.33 per cent. This represents in reality the irreducible fetal mortality and should form a base line in any study involving fetal mortality. Philosophically, it could be looked upon as the inherent or initial risk of being born. This fact emphasizes that even in a normal labor the baby undergoes some degree of intrauterine asphyxia.

Furthermore, had any of the mothers of these babies been given even the smallest amount of pituitary extract during their labors, it would, no doubt, have been considered that the fetal death had been due to the injudicious use of this drug.

TABLE XIV. FETAL MORTALITY, PRIVATE CASES, UNCOMPLICATED

TOTAL CASES: 717			CORRECTED FETAL MORTALITY
Erythroblastosis	2		
Congenital anomalies	4		
Baby dead on admission	4		
Intrauterine asphyxia		3	
Intracranial hemorrhage		2	
Total	10	5	0.69%

TABLE XV. BOSTON LYING-IN HOSPITAL, UNCOMPLICATED FETAL MORTALITY

TOTAL CASES: 636			CORRECTED FETAL MORTALITY
Fetal heart absent	4		
Prolapsed cord	3		
Von Gierke's disease	1		
Hemorrhagic disease	2		
Congenital anomalies	2		
Intrauterine asphyxia		2	
Intracranial hemorrhage		2	
Total	12	4*	0.63%

\*All cases in second stage labor for four hours each. Three cases had only 1 minim of pituitrin at full dilatation. One case had only 2 minims and total of minims 4 with full dilatation of cervix.

In Tables XIV and XV are listed the causes of fetal death in the private and clinic series in the uncomplicated groups. It can be observed that the fetal mortality was extremely low in those babies who theoretically should have been born alive. Again, intrauterine asphyxia was more outstanding than the problem of intracranial hemorrhage as a cause of fetal death.

Table XVI is the computation of the fetal mortality in all the series and groups in this study. Intrauterine asphyxia occurred four times as often as intracranial hemorrhage. This was even more impressive as the cause of death in those cases who were subjected to prolonged labor.

Of most importance is the high fetal mortality rate in the clinic series who were subjected to prolonged labor (complicated group, 11.65 per cent). This is about the fetal mortality rate that is generally reported in other studies

had ceased in the private patients, the drug was immediately given, while in the clinic series this was not necessarily true.

We have been impressed by the lack of accurate knowledge of the degree of the dilatation of the cervix in the complicated group of the clinic series when dilatation was slow or had entirely ceased. A great variation occurred in the recorded degree of dilatation of the cervix as determined by different examiners, even when the examinations were done simultaneously.

We feel that the routine use of the rectal examination can be very inaccurate in attempting to determine the degree of cervical dilation in patients who are making unsatisfactory progress. Pelvic examinations should be resorted to when there is any question of the degree of progress or lack of progress that these patients are making. It is only in this manner that accurate evaluation in changes of the cervix can be made, and a more intelligent understanding of the problem can be ascertained.

Furthermore, we have been impressed by the degree of dilatation of the cervix which occurs in patients who fail eventually to dilate their cervixes completely. With rare exception, cervical dilatation ceased in these cases when the cervix was between one-half and three-fourths dilated. So many times the cervix was thought to be nearly fully dilated by rectal examination, when on vaginal examination the above condition was found to exist.

It will be noted from this chart that the drug was administered in many of the private patients when the cervix was only half dilated. The criticism that severe injuries to the birth canal or that the drug is ineffectual when administered this early in labor is not substantiated by the results of this study.

*Fetal Mortality.*—(Stillbirth and neonatal deaths.) We have corrected the fetal mortality by eliminating premature infants (babies under 5 pounds), infants with congenital defects, erythroblastosis, or babies in whom the fetal heart was absent at the onset of labor. We have eliminated all the babies who were lost due to accidents of labor, such as prolapse of the cord. We have also eliminated babies who were lost because of antepartum bleeding due to premature separation of the normally implanted placenta and placenta previa, and babies who were born by breech extraction. There were six cases that were eliminated because of mid or outlet pelvic contracture, with associated difficult forceps, but not associated with prolonged labor. Two cases of prolonged labor which were not excessive in length and who showed no lack of progress, and, therefore, did not receive any posterior pituitary extract, were eliminated.

Table XIII represents babies who died for an unascrivable cause in the clinic during the past five years. This represents the large group of patients

TABLE XIII. UNASCRIBABLE CAUSES OF FETAL DEATH. NO POSTERIOR PITUITARY EXTRACT DURING LABOR

	ASPHYXIA	INTRA-CRANIAL HEMORRHAGE	AUTOPSIES	NORMAL DELIVERY	OUTLET FORCEPS	DELIVERY CASES	PER CENT MORTALITY	TOTAL
Stillborn	20	0	15	18	12	11,506	0.17	
Neonatal deaths	13	6	11	13	6	11,506	0.17	0.33

- Eliminate: (1) Premature and immature infants.  
(2) Congenital defects, erythroblastosis, absent fetal heart on admission.  
(3) Accidents of labor, prolapsed cord, and premature separation of placenta, etc.  
(4) Breech extraction.  
(5) Prolonged labor or difficult forceps, eight cases.  
2 cases: Prolonged labor, asphyxia.  
6 cases: Mid and outlet contracture, intracranial hemorrhage.

reminded that the amount of the drug was perhaps not used in doses which were sufficient to overcome this inertia. We would emphasize, however, that this group of cases illustrates the fact that the uterus may be or can become refractory to the drug.

In Table XVIII are listed the weights of babies in both series. It was thought that perhaps there was an increase in the average weight of babies which might have been a contributing factor in this type of dystocia. The over-all average was not significant when compared with a group of normal controls. However, there was a slight increase in the number of very large babies in the complicated group, and in those patients who were subjected to extraperitoneal cesarean sections.

TABLE XVIII. INFANTS' WEIGHTS

WEIGHT IN POUNDS	5 TO 6	6 TO 7	7 TO 8	8 TO 9	9	NOT RECORDED	TWINS	TOTAL
Private series, uncomplicated	36 6.0%	129 21.1%	247 40.5%	144 23.6%	54 8.8%	116	9	726
Boston Lying-in series, uncomplicated	37 5.6%	135 21.2%	231 36.2%	184 29.0%	52 8.1%		3	639
Private series, complicated	3	13	16	4	3	12	1	51
Boston Lying-in series, complicated	17 8.0%	38 18%	78 37.3%	56 27.3%	20 9.5%		3	209
Total cases	93	315	572	388	129	128	16	1,625
Normal control series	7.3%	21.8%	40.8%	24.3%	6.3%			

### Discussion

The problem of prolonged labor in the absence of cephalopelvic disproportion still remains one of the major problems in obstetrics. This is, no doubt, due primarily to the fact that we have no method of treating these cases which is entirely satisfactory. So little is known about the action of the uterus during labor. Little or nothing is known about why certain uterine contractions are effective and others fail to perform their normal function.

Measurements can be made of the types and frequency of uterine contractions, but of how much practical clinical value these methods may be for devising ways and means of treatment for these disturbing cases is debatable.<sup>2</sup> Until we know the physiologic cause of labor, we still must grope our way along in an attempt to treat this most stubborn of all obstetric conditions.

Two attitudes toward the treatment of these cases have been suggested. One is built around the idea that the patient will eventually deliver herself if subjected to enough hours of labor. The treatment is dependent primarily on general supportive measures. This involves the resting of the patient from time to time, usually with opiates, and keeping the patient in positive fluid balance by the use of much parenteral fluids. This is certainly in order in every case where the patient is not in true labor. Stimulation of labor during this time is truly contraindicated.

The second attitude follows the belief that once the patient has started in true labor (by this we mean that the cervix is beginning to dilate), progress should be definite and sustained until that patient is successfully delivered. To

TABLE XVI. CORRECTED STILLBIRTH AND NEONATAL MORTALITY

	NUMBER OF DEATHS	PRIMARY ASPHYXIA	CAUSE OF DEATH INTRACRANIAL HEMORRHAGE	PER CENT MORTALITY
Unascribable group	39	33	6	0.33
Private series, uncomplicated	5	3	2	0.69
Boston Lying-in series, uncomplicated	4	2	2	0.63
Private series, complicated	2	2	0	4.00
Boston Lying-in series, complicated	24*	20	4	11.65

\*Five deaths were associated with 17 cases of Dührssen's incisions.

of the effect of prolonged labor on the infant irrespective of the type of treatment employed. It is this group which truly represents the effect of prolonged labor on the infant. We have failed to treat properly such cases. It is well if we are to try to improve the treatment of these cases to evaluate carefully the factors which have contributed to such failures.

TABLE XVII. FACTORS IN THE STILLBIRTH AND NEONATAL MORTALITY.  
BOSTON LYING-IN COMPLICATED GROUP

24 cases		(3) Prolonged labor without lack of progress	(5) Reasons for lack of progress
(1) Abnormal pelvis	7	(4) Prolonged labor with lack of progress	a. contracted outlet 3
(2) Prolonged labor		a. 10 to 20 hrs.	b. inertia 19
a. 20 to 40 hrs.	17	18	
41 to 60 hrs.	3	4	
60 hrs.	4		

In Table XVII is listed some of the factors which have contributed to such a fetal mortality in the complicated clinic series. Borderline pelvis were perhaps a contributing factor in seven cases. Prolonged labor, per se, was, of course, the outstanding factor. Of most interest in this respect are the seven babies who were lost in patients who were subjected to labors of more than forty hours' duration. When we consider that only 26 cases in the entire clinic series were subjected to over forty hours of labor, this leaves us with a fetal mortality in the particular group of 29 per cent.

However, there are other factors which contribute not only to this fetal mortality, but also to the initial fetal mortality of 11.65 per cent. One of the most outstanding is the lack of progress prior to delivery which had occurred in those labors where the babies were lost. Not only do we have the factor of prolonged labor, but in addition we have what we believe is a most important factor, namely, the many hours of labor that were allowed to elapse even in the absence of any increase in the dilatation of the cervix. In other words, we not only subjected the patient to many hours of labor, in these cases where babies were lost, but we have subjected them to many hours of some sort of labor after progress had ceased. In 22 of the 24 babies lost, 18 were subjected to from ten to twenty hours of additional labor without progress, and four other babies were subjected to twenty hours or more without progress. This would suggest that this is one of the most important factors contributing to the high fetal mortality in this complicated group of cases. Even if a difficult pelvic delivery were anticipated in these cases, "watchful waiting" was not necessarily the correct procedure.

It will be further seen that the causative factor in this lack of progress was attributed to uterine inertia. Although pituitrin extract was used, one is

becomes one-half to three-quarters dilated. Posterior pituitary extract will be given without effect. The patient still makes little or no progress, and many valuable hours elapse in which the baby in the meantime is suffering from an increasing degree of intrauterine asphyxia. After a period of twelve to twenty or even forty hours has elapsed with no further progress, the patient is finally delivered by either Dührssen's incisions or extraperitoneal cesarean depending upon the degree of dilatation of the cervix, estimated size of the infant, and finally, evaluation of the pelvis, particularly in regard to the capacity of the midpelvis and the pelvic outlet. It should be emphasized that this is the usual sequence of events when the so-called conservative policy is pursued, and where posterior pituitary extract is not used. The fetal mortality associated with such a course in labor (however treated) raises the problem of whether we can better our results by a more rational policy of treatment.

Before we suggest such a policy of treatment, there is one group which deserves special comment. It will be seen in Table III that in the complicated clinic group the number of multiparous patients who were given posterior pituitary extract was extremely small. Criticism of giving these patients pituitary extract is valid, for it seems most reasonable that a patient who has successfully dilated the cervix in a previous labor should be able to do it again. However, there are those that believe that the entity of cervical dystocia does not exist, but that the problem is one of inertia. This is difficult to reconcile because it appears that once the cervix becomes completely dilated or is incised (Dürrssen's incisions), dilatation of the cervix in subsequent labors is never a problem if there is no cephalopelvic disproportion. If inertia plays the dominant role in these, why do we not seem to observe it in subsequent labors?

To emphasize this point of view, it will be noted that only one out of seven cases of prolonged labor occurring in the multiparous patients was caused by uterine inertia per se (Table III). Unrecognized cephalopelvic disproportion was at least in part a contributing factor in their dystocia. In other words, these cases composed a small group of the occasional but extremely important group of so-called "dangerous multiparas." These are individuals who had previous pelvic deliveries with living children, the babies usually being small or, at best, average in size. During the pregnancy in question the pelvis had not been properly evaluated. The babies were much larger than any they had previously delivered. This factor, combined with borderline or a definitely abnormal pelvis, resulted in a dystocia on the basis of cephalopelvic disproportion. In other words, inertia associated with cervical dystocia is a syndrome restricted with rare exception to primiparous women. This suggests that any multipara who is in true labor and does not deliver herself before twenty hours after the onset of labor should be regarded with great suspicion. Other factors, such as contracted pelvis, abnormal presentation, or extremely large infants, may be the cause for the dystocia. Failure to recognize and properly treat such a group may well be the source of most of the cases of spontaneous rupture of the uterus. Stimulation of labor in the multiparous patient who is experiencing prolonged labor should be done with great caution, and only after careful observation regarding the above factors.

suggest the use of posterior pituitary extract as the means of producing sustained progress in the labor of such patients is looked upon by many as a very questionable procedure. Those who would condemn the drug cannot see any rationale for its use. They condemn it because they believe that when it is used in the first and second stages of labor, great trauma is produced to the birth canal as well as possible severe intracranial damage to the infant.

The literature in expression of these opinions is voluminous. Reports of rupture of the uterus, birth trauma to the infant, are always reported as being due to the use of this drug, and for the most part many of the other factors are ignored. Many of these cases so reported of severe trauma to the birth canal do not make it clear whether the problem of cephalopelvic disproportion was considered. In any event, to condemn a drug purely because it is not used properly is an unscientific approach.

We believe that the drug, posterior pituitary extract, can be administered safely during labor. From this report we believe that we have demonstrated that it is possible to give posterior pituitary extract in the first and second stages of labor without undue harm to either mother or baby. We believe that it has, like many drugs in medicine, its demerits as well as its merits. We have not been so impressed by its dangers as by its limitations. These limitations are due primarily to the fact that in certain cases of prolonged labor, a desired physiologic effect is not always obtained with its use.

Certainly we have decreased the incidence of prolonged labor, and in doing so, we have not produced any deleterious effect on mother or baby. Knowing the relatively high fetal mortality which accompanies prolonged labor, we feel that if it is possible to decrease the incidence of this syndrome that this very definitely justifies the use of the drug. The incidence of prolonged labor varies in different clinics, but in this clinic for the past five years when the drug has been used in inertia cases, prolonged labor has occurred in only about 2 per cent or even less in all cases delivered. This is two to five times less frequent than the usual incidence quoted for this complication. Midforceps operations have been done only 56 times during this five-year period, which is an incidence of 0.5 per cent. This operation is being done four to eight times less often than the incidence is usually reported. The use of Dührssen's incisions have been limited. In those cases where this operation was necessary, the fetal mortality was high (30 per cent). This is not to condemn this procedure. The results with this operation might have been improved had we resorted to it earlier in the course of a given labor after progress had failed to occur after a reasonable time.

We feel that our mistakes in using posterior pituitary extract have occurred because we have failed to appreciate fully that the drug will not produce progress in all patients. Furthermore, we have failed to realize that the drug could be used in larger initial and total doses in order to insure sustained progress. This is emphasized by the increased dosage used in the private series in contrast to the clinic series.

The failures which have occurred appear to follow a very definite pattern in these cases of prolonged labor. First, progress usually ceases when the cervix



to three hours) it seems reasonable then to discontinue the drug and turn to other means of completing labor. Procrastination from that point on will only add further hours of labor with its accompanying increased fetal mortality.

### Conclusions

1. Prolonged labor, dependent on uterine inertia and associated with cervical dystocia, is a syndrome occurring with rare exception only in primiparous women.

2. Such exceptions are not due to cervical dystocia per se, but many occur in the "dangerous multiparas" with definite or borderline cephalopelvic disproportion.

3. We have administered posterior pituitary extract to 1,609 patients who exhibited any degree of uterine inertia during their labor.

4. The initial dose of this drug was usually one minim. The dosage was increased up to four minims at a single dose in an attempt to stimulate uterine contractions. Usually cervical dilation would ensue with the smaller doses.

5. The total dose in a given labor was usually one to four minims, but doses from five to nine, ten to fifteen, and even fifteen minims plus were administered during a single labor.

6. With the use of this drug there have been no cases of ruptured uterus or extensive birth canal trauma in this series.

7. The incidence of prolonged labor has been reduced to the low figure of 2 per cent in the clinic patients.

8. The need for midforceps operations in the clinic patients was reduced to 0.5 per cent. The need for Dührssen's incisions was small.

9. Some degree of intrauterine asphyxia accompanies normal labor. In this series it was 0.33 per cent.

10. Prolonged labor contributes materially to an increased fetal mortality. This is particularly true if more than forty hours in length.

11. Fetal mortality in the clinic patients with prolonged labor was 11.65 per cent, a figure which usually accompanies such cases. Intrauterine asphyxia was the most frequent cause of fetal death.

12. An attempt to evaluate the factors which contributed to this fetal mortality have been analyzed.

13. A policy in handling cases of prolonged labor with special regard to the use of posterior pituitary extract has been presented.

The author wishes to thank Dr. Frederick C. Irving for the use of his personal records which represent the patients reported as the "private series."

### References

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2. Murphy, D. P.: *AM. J. OBST. & GYNEC.* 41: 274, 1941.

On the other hand, it seems reasonable that a more rational method of attack might be suggested for these primiparous patients undergoing prolonged labor. If one is willing to concede that progress is imperative in all cases in which the patient has committed herself to dilatation of the cervix (true labor), then we are confronted with the problem of how best to carry out such a program. If one can see any merit in the use of posterior pituitary extract, then it would seem possible that we should be able to suggest a policy whereby it could be put to its most effective use.

In these patients who are experiencing prolonged labor in the absence of cephalopelvic disproportion, it is essential that degrees of progress should be measured carefully. As has been stated, rectal examination oftentimes is inaccurate, and frequently it is much better to resort to a sterile pelvic examination to ascertain the exact degree of dilatation of the cervix. This is particularly true if one is convinced that progress is not being made. It is only in this manner that one can date accurately the time in which progress has ceased. From this study we feel that lack of progress over twelve hours is not only detrimental, but may be lethal to the infant. We believe that the twelve hours which will elapse after progress has ceased is the most important time of the patient's labor.

This is the time which should be utilized for the stimulation of labor. If one desires to use posterior pituitary extract for such stimulation (and this seems to be the only effective means which one can employ), then a definite method of treatment can be outlined.

We shall administer pituitary extract for at least two reasons. First, to give the drug in the hopes of producing progress, as denoted by further dilatation of the cervix. Second, to attempt to ascertain whether we can expect progress. By this is meant that if the uterus is refractory to the drug, is it not reasonable to say that the uterus is refractory to further progress of labor. Assuming this to be true we can then start with the premise that we are giving the drug in increasing doses in order to produce progress, or, having given a reasonably large dose without effective progress, we can then turn to other means of terminating the labor. In this manner we have demonstrated in a comparatively short period of time that further progress will not take place. In this way we not only save the mother many hours of nagging uterine contractions which are ineffectual, but we have perhaps saved the fetus from irreversible damage. It is suggested, therefore, that we will give this drug in cases of prolonged labor as close to the time that progress has ceased as possible. The dosage should start with minim one and increase minim one every thirty to forty-five minutes until effective uterine contractions are produced. This dosage should increase, if necessary, up to a four-minim dose at a single dose. The size of the dose, of course, is regulated by the effect. Effective uterine contractions may ensue with the initial dose, and, in like manner, no effect may be obtained by a larger dose. However, if no effective uterine contractions or progress has been obtained after one to four minim doses have been used (which will cover a period of from two

Vozza<sup>8</sup> found correlation between the changes in potential and the contraction wave in experimental animals, but he too found some deflections of the string which were not associated with obvious muscle contraction. In 1935, Falk and Nahon<sup>9</sup> described action currents taken from the uterus of the human by an intrauterine silver electrode, and found that these currents could be definitely correlated with the ovarian cycle. Jacobson and co-workers extended these findings.<sup>10</sup>

Up until this time the electrical activity of the organ had been determined by the string galvanometer of Einthoven or a modification. The need for the study of the direct current components of smooth muscle activity has long been recognized, and Burr and associates<sup>11</sup> emphasized the requirements of any direct current amplifying system in the study of smooth muscle potentials, and described the changes occurring in uterine activity in association with the ovarian cycle.<sup>12</sup>

A great deal of work on smooth muscle has been done by Bozler,<sup>13-15</sup> who has shown that the contractions of the smooth muscles of laboratory animals are accompanied by bursts of impulses which are biphasic and carry a potential of one to two millivolts.

Our interest in the problem of the electrical phenomena associated with contractions of uterine muscle arose when planning a study of the physiology and pathology of labor. It seemed reasonable to suppose that the functional and conduction defects of the heart in severe myocardial damage, abnormalities of the bundle of His, and others, might well have a uterine counterpart. With this in mind, a systematic trial of some of the more likely methods of amplifying and recording electrical currents was instituted, and the findings are presented.

### Materials and Methods

Evidence of electrical activity taken from the uteri of laboratory animals has demonstrated high frequency changes in potential associated with muscle contraction, and published curves also show a slow and maintained deflection of the string from the base line as do studies of the human uterus. It was therefore felt that investigation with both alternating and direct current amplifiers and recorders would be necessary in order to clarify the part played by each component.

The first alternating current amplifier and recorder used in the investigation was the portable electrocardiograph. This instrument is essentially a vacuum tube amplifier which responds uniformly to frequencies of one to 50 cycles. The recording is made on rapidly moving photographic film by an oscillograph driven by a resistance-condenser coupled amplifier. A one millivolt input signal causes a deflection of 10 mm. of the light beam. German silver metal plates, 4 by 5 cm., and electrode paste to reduce polarization and improve contact with the skin, were used. One electrode was placed just lateral to the umbilicus and the other (indifferent electrode) on the upper portion of the thigh.

The portable electroencephalograph\* was the other alternating current amplification method used. It is a five-stage resistance capacity coupled ampli-

\*This instrument was furnished by Dr. Paul Traugott of the Electro-Physical Laboratories, 25 West 18th Street, New York, New York.

## THE ELECTRICAL POTENTIALS OF THE HUMAN UTERUS IN LABOR\*

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IT MAY seem odd that an anatomist should discover electricity, but when Luigi Galvani touched frog muscle with a charged metal plate and found that it twitched, a broad and profitable field of medical investigation was opened. It remained for Volta, Oersted, and Einthoven<sup>1</sup> to develop means of measuring the force of this phenomenon, but once the galvanometer was in common use, its application for recording the electrical potentials accompanying activity of the heart, striated muscle, and brain was merely a matter of time.

Electro-investigation of the smooth muscle containing organs, however, has lagged far behind because of at least three factors: the structures are relatively inaccessible, the voltages emitted are small, and the interpretation of the findings has been exceedingly difficult.

One of the earliest investigators to study the uterine electrical phenomena was Theilhaber,<sup>2</sup> who, in 1910, thought he had found a significant difference in the action of the string galvanometer in women whose uteri and ovaries were intact as differentiated from those after the menopause or following hysterectomy. Metal electrodes were used, one on the cervix and the other in the rectum. Veit,<sup>3</sup> a few years later, was unable to detect uterine currents by applying one metal electrode to the arm and another to the leg, but obtained large deflections from the cardiac cycle. Blumenfeldt and Dahlman,<sup>4</sup> attempting to correlate changes in potential from the uterine horns with the mechanical action of the uterus as determined by a balloon in the cavity, were able to obtain definite deflections of the galvanometer string coincident with the uterine contraction (mechanically produced), but stressed the fact that in some instances voltages varied without corresponding muscle contraction.

More than ten years passed before further attempts were made to clarify the problem. In 1928, Greene<sup>5</sup> found that the galvanometer deflection which accompanied muscle contraction had a high frequency and that the amplitude of the deflection increased as the contraction gained strength, and Hasama,<sup>6</sup> in 1930, using Zn-ZnCl electrodes directly on the rabbit uterus, was able with the string galvanometer to record deflections of over a millivolt with a frequency of 10 to 15 cycles per second. Bode,<sup>7</sup> in 1931, using the string galvanometer and metal electrodes which were standard for electrocardiography at that time, placed the electrodes on the abdomen at the level of the umbilicus, and during labor noted a deflection of the string during the contractions of labor with a degeneration of the deflection as the uterine tone decreased. This seems to be the only report of an attempt to record changes in electrical potential from the human uterus in labor.

\*The opinions expressed here are those of the authors and do not necessarily reflect those of the Navy Department.

These tracings are fairly characteristic of what is observed by this type of amplification and recording. Tracing *B* seems the only one of note if a departure of the galvanometer from the normal pattern is sought; its configuration is not unlike that reported by Bode.<sup>7</sup> No high frequency components are noted here that are not ascribable to the maternal or fetal cardiac current, but only a slow departure from the base line, denoting a change in potential of low frequency. However, since no large deflections of this type were noted under a general anesthetic, it would be reasonable to suppose that it was an artifact due to voluntary muscle contraction, despite the fact that the patient produced no obvious undue motion.

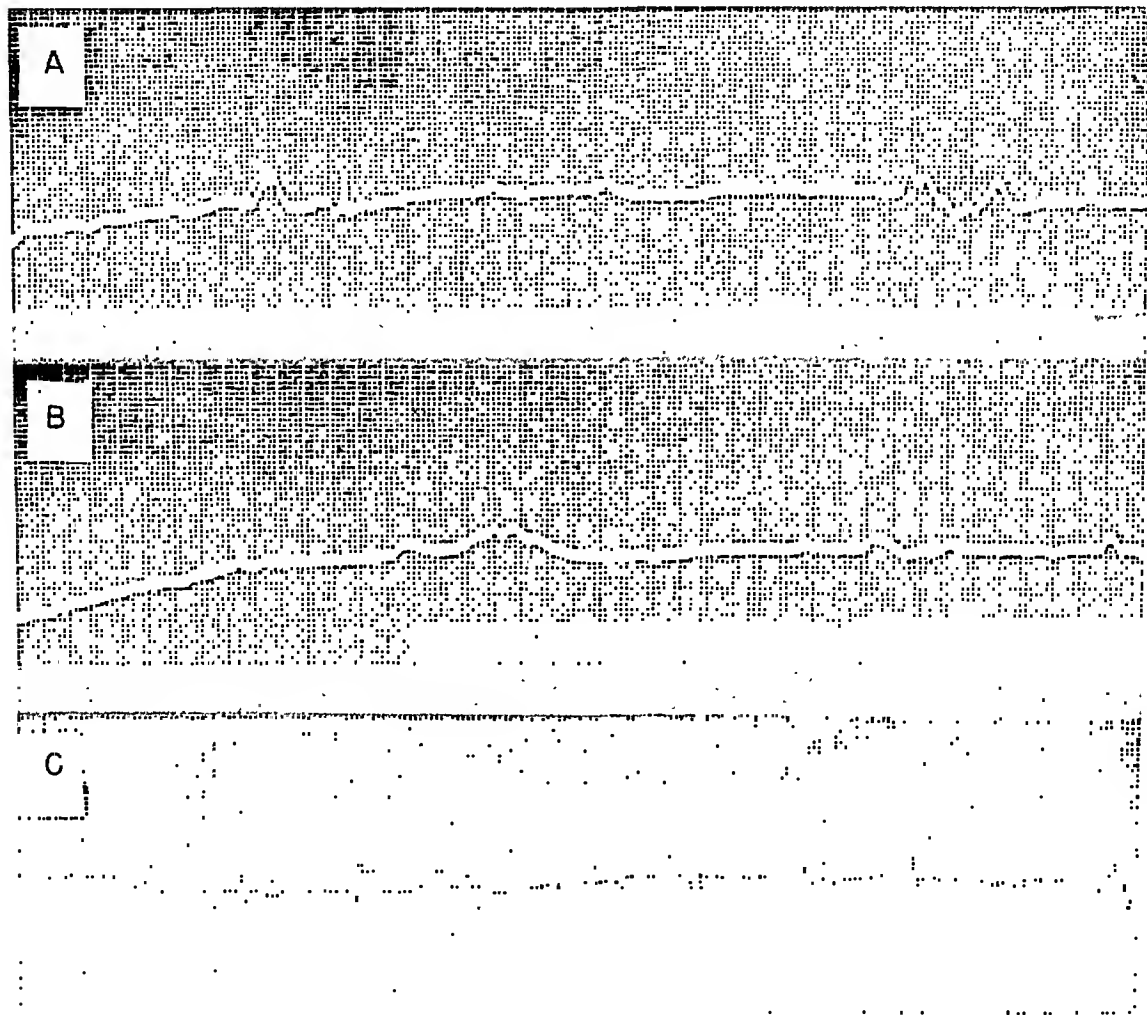


Fig. 1.—Tracings taken by the portable electrocardiograph.

*A.* This tracing was taken during labor but while the uterus was relaxed. There was no analgesia.

*B.* During this period the uterus was contracting strongly. There was no analgesia.

*C.* The uterus during this tracing was contracting strongly. The patient was lightly anesthetized by ethylene and oxygen and all voluntary muscular action was reduced to a minimum.

*Group Two.*—Obtained by the electroencephalograph. One patient.

In order to be more certain that high frequency changes in potential were not being missed through a lack of sensitivity of the recording mechanism, an electroencephalograph was used on one patient. Fig. 2 shows the result of this attempt.

fier which, with filters on, records accurately within the range of one to 35 cycles per second and gives a deflection of one centimeter with an input signal of ten microvolts. The deflections are recorded by magnetically driven inking pens upon a uniformly moving paper roll. The electrodes used were solder pellets 7 to 8 mm. in diameter, coated with electrode jelly and made adherent with collodion and adhesive tape. One electrode was placed lateral to the umbilicus and the indifferent one placed on the upper portion of the left thigh. The instrument was suitably grounded.

In order to determine electrical activity which might occur at a frequency of less than one cycle per second, it was found necessary to search for a suitable direct current amplifier and recorder. The vagaries of this type of amplification are well known, and only after much difficulty was an instrument obtained. This amplifier is a vacuum tube direct current amplifier with moderate sensitivity, high input impedance, with enough output to drive a pen-writing instrument.† The recorder is a sensitive magnetically-driven pen which records on a calibrated paper at a rate of 3 inches per minute.‡ This combination of instruments produces a deviation of the writing pen of one-half inch for an input signal of one and one-half millivolts. Drift is not negligible but is at a minimum for this type of amplification, and the pen of the recorder responds sluggishly to any input frequency of more than one cycle per second. Electrodes are fluid (.85 per cent sodium chloride in distilled water) to prevent polarization, and contacts are platinum. The area of skin contact was encircled with collodion to prevent changes in area with stretching of the abdominal wall. The platinum lead wires to the electrodes were attached to the amplifier through shielded copper wires, and the instrument was suitably grounded.

Patients at term in all stages of labor and prelabor were utilized in this investigation. All were volunteers, were cooperative, and were impressed with the necessity of restriction of voluntary motion.

### Results

*Group One.*—Obtained by the portable electrocardiograph. Six patients.

The records obtained by the portable electrocardiograph, using metal electrodes, one placed on each side of the umbilicus, are represented by the tracings in Fig. 1.

Tracing *A* represents the effect of the uterus in labor but in the absence of a contraction. The fetal and maternal electrocardiograms are seen and voluntary muscle effects are in evidence.

Tracing *B* was taken from the same uterus during a contraction and shows an initial upward deflection of the galvanometer. The patient was moderately comfortable during this contraction; she made every effort to cooperate in avoiding voluntary motion and none was obvious to the observers.

Tracing *C* shows the action of the galvanometer during a contraction in which the patient was under ethylene anesthesia, carried to a sufficient degree to obliterate all voluntary motion, but still sufficiently light to allow the uterus to contract spontaneously.

†This is a Type 715-A direct current amplifier manufactured by General Radio Company, Cambridge, Massachusetts.

‡This is the Esterline Angus supersensitive recorder in which one milliampere gives a full scale deflection.

Here as in the records made by the electrocardiograph there is no clear cut evidence of high frequency components accompanying the muscular activity of the uterus.

*Group Three.*—Obtained by direct current amplification. Ten patients.

Figs. 3, 4, 5, 6, and 7 show tracings obtained on patients by the direct current amplification method described.

Because of the excessive "drift" which occurs in most direct current amplifiers, frequent control runs are made throughout the period of observation. Tracing A (Fig. 3) represents such a control for the drift of the instrument. This was taken from the abdomen of a nongravid woman at rest.

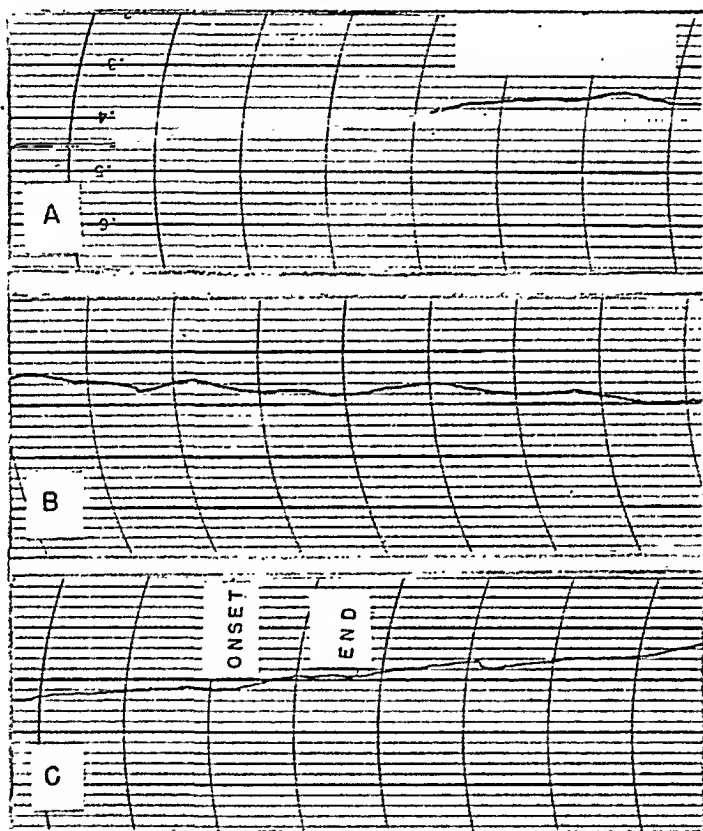


Fig. 3.—Tracings obtained by the direct current amplifier.

A. Deflections noted with the electrodes on the control abdomen (nonpregnant) at rest with no anesthesia or pain.

B. This tracing was taken from the abdomen of a pregnant woman at term with no contractions evident.

C. Contractions had just begun, were painless and irregular, at the time of this tracing.

Tracing B (Fig. 3) is also a control record, using the abdomen of a patient with a term pregnancy, but not in labor.

Tracing C is a record taken on the same patient a few hours later, after rupture of the membranes to induce labor. Contractions of a mild type were noted, painless, fleeting, and of nondescript character.

Tracing A of Fig. 4 demonstrates the typical painless contractions of a definite nature which are known as Braxton-Hicks contractions.

Tracing B (Fig. 4) was taken after the patient was in moderately severe labor. This patient was extremely cooperative, had no sedation at this point, and was as well "relaxed" as is reasonable under this type of labor.

Tracing *A* represents the activity recorded from the uterus of a patient actively in labor but with no contraction at the time of this tracing. The maternal and fetal electrocardiograms are again in evidence, and a minimal amount of voluntary muscular activity.

Tracings *B* and *C* were taken during a moderately severe contraction during which there was a minimal amount of voluntary muscular activity on the part of the patient.

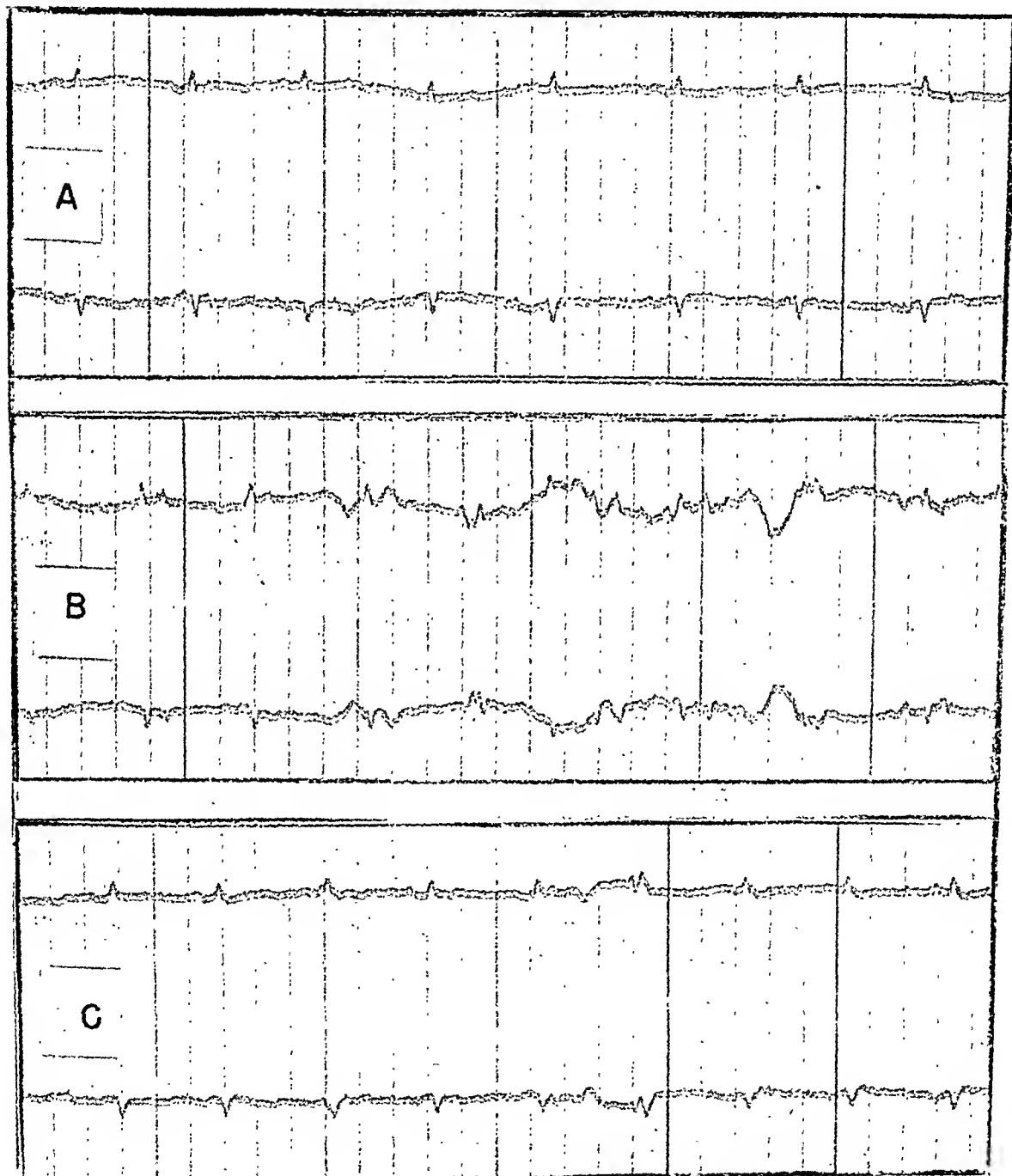


Fig. 2.—Tracings taken by the portable electroencephalograph.

A. This tracing was taken in labor while the uterus was relaxed between contractions.

B. This tracing represents the uterus actively contracting.

C. This tracing was also taken during an active contraction.



Tracing *C* (Fig. 5) was taken on a patient who had had fourteen hours of severe "driving" labor while overcoming a moderate disproportion between the head and pelvis. The rapidity of onset of these contractions and their long duration is noteworthy.

Fig. 6 is designed to show the great difference in the tracings obtained under caudal anesthesia and those obtained without analgesia. It should be emphasized that morphine, scopolamine, the barbiturates, and rectal ether were all considered but were discounted because the patient who is moderately or heavily sedated is unable to cooperate, and enough of these drugs to produce loss of all motion would be unsafe.

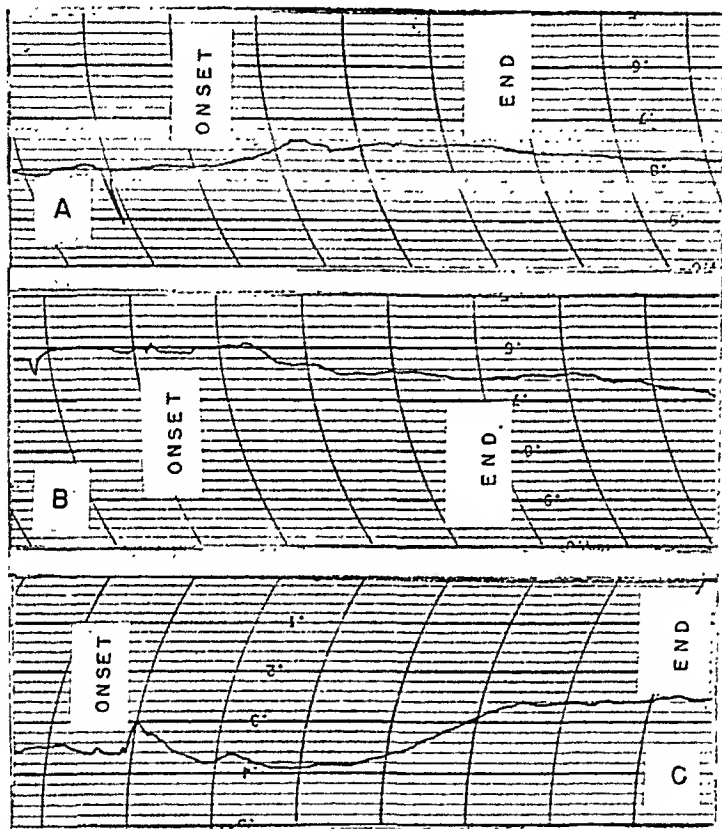


Fig. 5.—Tracings obtained by the direct current amplifier while the patients were made completely oblivious of pain during the uterine contractions by caudal anesthesia.

A. This tracing was made upon a patient in moderate early labor, and cervical dilatation was slow.

B. This patient was having firm contractions and the cervix was dilating rapidly.

C. This tracing was taken at the end of the first stage of a patient in a severe driving labor in which there was mild cephalopelvic disproportion.

Tracing *A* shows the drift of the instrument under laboratory conditions, with no electrodes on an individual but merely connected across a 10,000 ohm resistor. The  $1\frac{1}{2}$  millivolt standard was used to produce the standard deflection.

Tracing *B* (Fig. 6) shows two consecutive contractions and the interval on a patient without sedation.

Tracing *C* (Fig. 6) shows the same type of labor in a patient with caudal anesthesia.

*Group Four.*—Obtained by direct current amplifier at cesarean section with electrodes on the uterus.

Tracing *C* (Fig. 4) was taken after the patient had been lightly anesthetized by ethylene-oxygen anesthesia. There was good relaxation, and voluntary muscle ability was abolished, but the uterus was still contracting.

When caudal anesthesia was utilized, several very obvious differences were noted in the tracings. The greatest was the absence of vast changes in the overall potential obtained. In these patients the deflection caused by a contraction was a departure from a relatively straight line, while in the patients feeling pain during the contractions, the deflections of the contraction were larger but were accompanied by such huge changes in skin potential that many times they were dwarfed.

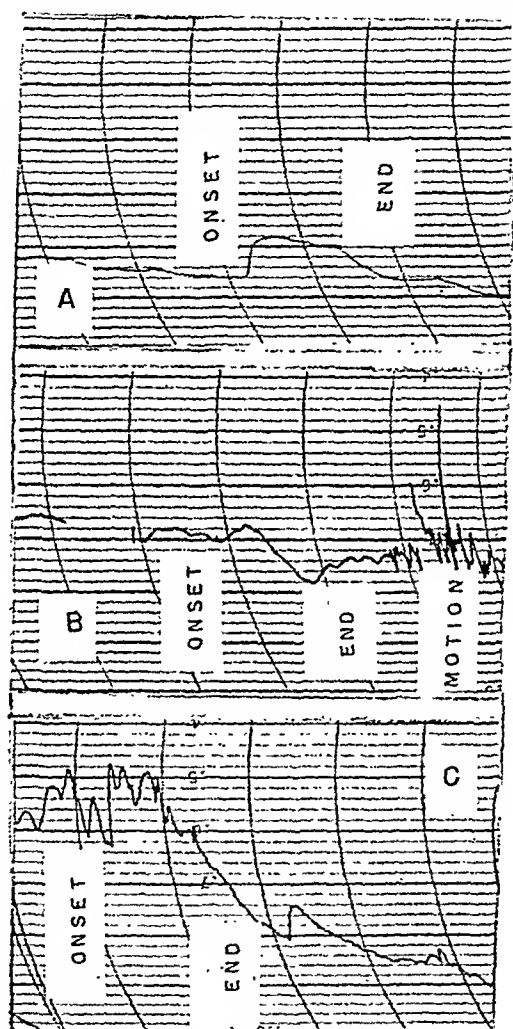


Fig. 4.—Tracings obtained by the direct current amplifier under no analgesia.

A. Contractions here are still painless but regular, and the uterus is moderately firm to palpation.

B. The contractions represented by this tracing accompanied early labor. The uterus was moderately tense.

C. This patient was in the second stage of labor and contractions were of good quality. The record was taken under light ethylene anesthesia.

Fig. 5 demonstrates tracings taken under caudal anesthesia. Tracing *A* was taken immediately after the inception of the caudal anesthetic when the contractions were mild, irregular, and had little effect in producing cervical dilatation.

Tracing *B* (Fig. 5) demonstrates the change in potential produced by the same uterus during hard contractions of such a nature that the cervix attained full dilatation in one-half hour from an initial five-centimeter stage.

This curve (A) is an electrical deflection produced by a pituitrin-induced contraction. The patient was under light ethylene anesthesia and was given 3 minims of pituitrin intramuscularly.

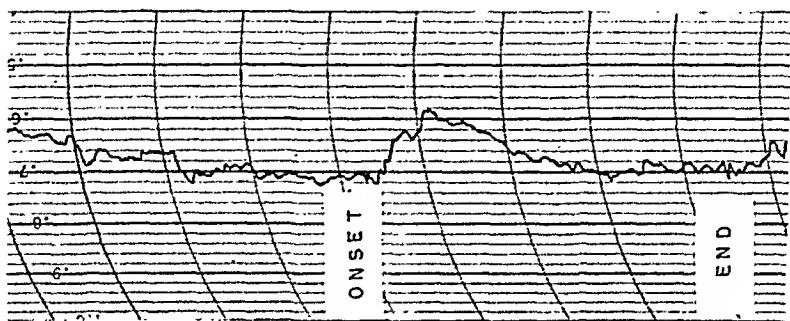


Fig. 7.—This tracing was obtained by the direct current amplifier directly from the uterus at cesarean section. The patient was lightly anesthetized by ethylene and a pain induced by pituitrin (3 minims intramuscularly).

### Discussion

Under the conditions of this experiment we have been unable to find any significant variations in potential associated with the contractions of the smooth muscle of the human uterus during labor in the frequency range above one cycle per second. Trial with the electroencephalograph was not as extensive as is desirable but with the portable electrocardiograph, even with the leads on the uterus, no high frequency components were noted.

Low frequency variations in potential are obtained from the anterior abdominal wall. Although voluntary muscle factors may cause many of the large changes seen in patients feeling pain from uterine contractions, definite deflections are obtained under caudal anesthesia and general anesthesia, where striated muscle effects must of necessity be at a minimum. Similar changes are noted when the electrodes are placed directly upon the uterine surface, although they are much more sharply defined and of higher amplitude.

There are several disturbing features, however: the apparent lack of uniformity of the method of spread of this current over the uterus, the deflections noted between contractions, which rarely may have as much potential as those accompanying contractions, and other technical details having to do with the lack of stability of the instrument and the interfering voluntary muscle effects. Malpas<sup>16</sup> has shown by direct observation of the uteri of patients under spinal anesthesia that in late pregnancy the uterine fundus contracts in a mass. This and the pattern of electrical conduction which we have observed may mean that there is no constant pacemaker or specific conduction pattern in this organ. Further investigation with different electrode positions will be necessary to clarify this point.

Exactly where this method of investigation will fit into the study of the physiology and pathology of labor remains to be seen. It does seem to be true that weak and inconsequential contractions produce less voltage than severe contractions. The pattern of the change in potential both during and between contractions is too confusing at this time even to allow speculation.

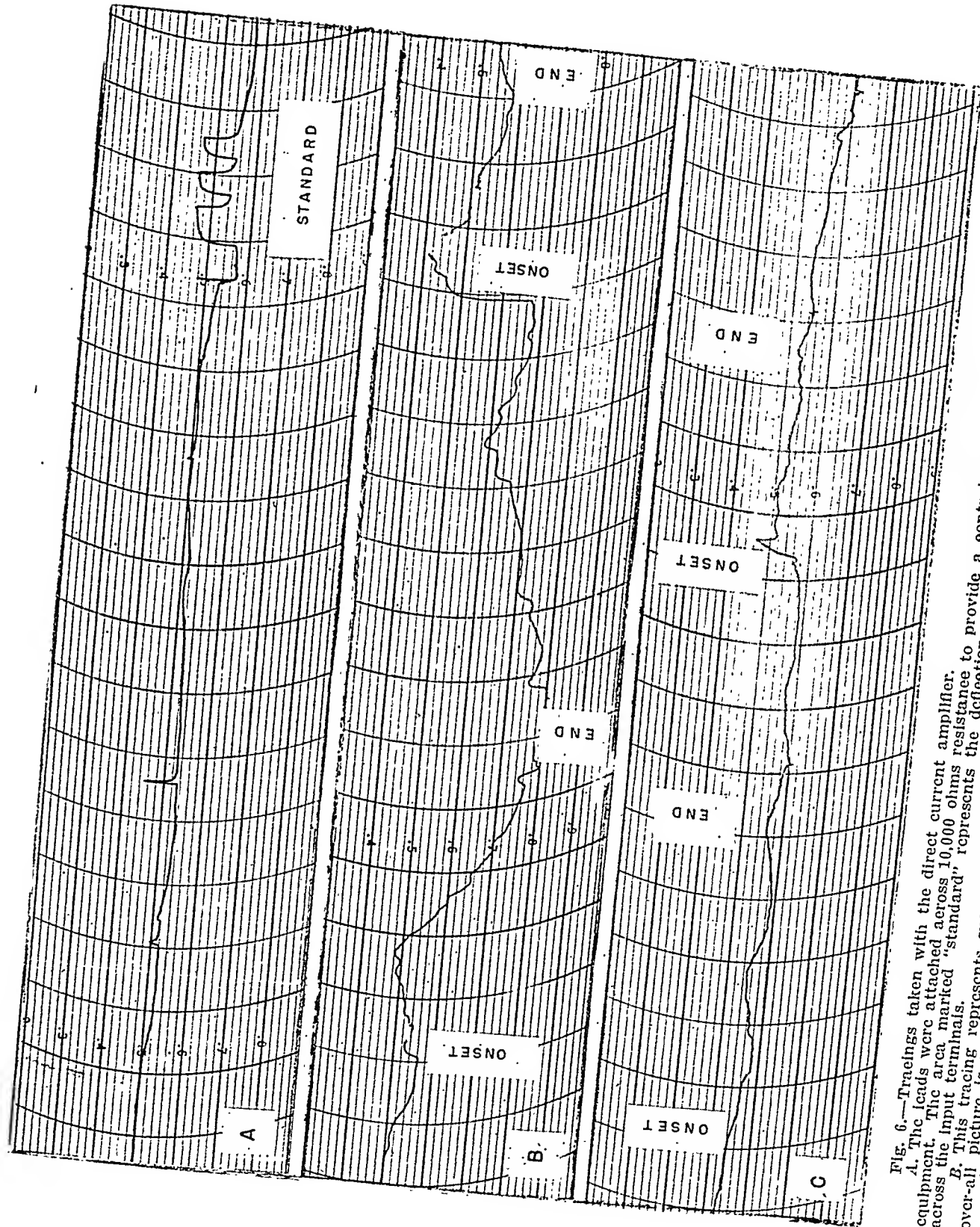


FIG. 6.—Tracings taken with the direct current amplifier.  
A. The leads were attached across 10,000 ohms resistance to provide a control for calculation of "drift" inherent in the equipment. The area marked "standard" represents the deflection produced by the application of one and one-half millivolts across the input terminals.  
B. This tracing represents successive contractions of the uterus in active labor. This patient had no sedation. The over-all picture is presented and the action of the recorder between contractions is evident.  
C. This tracing is taken from a patient having the same type of labor but experiencing no pain because of the caudal anesthesia. Note the huge difference in the over-all pattern.

## THE FOURTH STAGE OF LABOR\*

### An Account of the Physiology and Clinical Aspects of the Postpartum Uterus During the First Postplacental Hour

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*"There is no more startling or fearsome thing in the practice of obstetrics than an unexpected, serious, postpartum hemorrhage."* (Titus<sup>1</sup>)

THE sequence of intrauterine events which transpire during the postplacental hour comprises a distinct physiologic and clinical entity. Their collective recognition as the "fourth stage of labor" would help save the lives of those mothers who die of mishandled postplacental hemorrhage and spare the survivors the complications of sepsis and anemia that lie in its wake.

As the sulfonamides and antibiotics seal the doom of puerperal infection, puerperal hemorrhage will eventually take first place among the causes of maternal mortality. And as the attempts to combat puerperal hemorrhage gain in momentum, the critical first postplacental hour will necessarily have to be accepted as a normal part of every labor; for, as a series of individual but inter-related physiologic components, the fourth stage of labor will have to be recognized and treated with understanding, lest one of its components rebel under maltreatment, go berserk, and cause destruction.

Dieckmann,<sup>2</sup> in 1935, stated, "... obstetric hemorrhage is of great import, and despite our voluminous and occasional enthusiastic reports of the treatment of these various conditions, the mortality has not decreased in the past twenty years. What is the explanation for this appalling mortality?"

A five-year maternal mortality study for the years 1935 to 1940 in the city of Buffalo<sup>3</sup> showed hemorrhage to be still in the background; true, it caused the death of 64 mothers, which was 20 per cent of all maternal deaths; but it was second only to puerperal sepsis which, in the early days of sulfonamide therapy, was still able to be queen of the causes of maternal death. As in Buffalo, so throughout the world, sepsis served to distract obstetricians from the "broad stream of blood" that ran through the morbidity and mortality statistics of postpartum pathology ever since Man exchanged a rib for the uterovaginal tract.

In a later study, conducted in the Borough of Brooklyn of the City of New York, the trend from sepsis to hemorrhage is clearly seen. This seven-year report of the major causes of maternal mortality in that densely populated part of Greater New York, from 1937 to 1943, shows that hemorrhage superseded both infection and toxemia (Fig. 1); it was thus concluded by Gordon, that "hemorrhage is the outstanding controllable factor in maternal mortality."

On the basis of that study, Gordon<sup>4</sup> contended that "preventive measures for reduction of maternal mortality will produce greater results if emphasis is placed on hemorrhage rather than infection. At present, hemorrhage is the most important cause of maternal death, and probably the most common as well."

\*This paper is based on observations made by the author while he was Resident Physician in Obstetrics and in Obstetrics and Gynecology at the New York City Hospital, New York Beth Israel Hospital, and at the Buffalo General Hospital.

### Summary

Contraction of the uterine muscle during labor in the human is accompanied by changes in potential of low frequency and voltage.

Voluntary muscular activity, the apparent lack of identical or even similar conduction patterns, and the technical inherent difficulties of the amplification of direct current all make a great deal of investigation necessary before the procedure can be properly evaluated in respect to its status in the labor problem.

The authors wish to thank Dr. G. J. Ellis, Dr. J. B. Sheffery, and Dr. Catherine Johnson of Providence Hospital, Washington, D. C., Dr. Thomas Leonard and Dr. William Lady of Gallinger Hospital, Washington, D. C., and Dr. J. W. Pearson of the United States Naval Dispensary, Bellevue, D. C., for help on this problem.

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TABLE I. MAJOR CAUSES OF MATERNAL DEATH  
BROOKLYN, 1937-1943

YEAR	INFECTION	TOXEMIA	HEMORRHAGE
1937	27	26	29
1938	27	18	27
1939	30	12	14
1940	18	10	28
1941	10	8	20
1942	25	22	30
1943	13	14	60
Total	150	110	208

A recent study of all maternal deaths in the viable period of pregnancy in the Borough of Manhattan of the City of New York, by a special Committee of Maternal Welfare, "reveals the startling fact that more than one-half of all maternal deaths during this period of pregnancy are due directly to hemorrhage or that hemorrhage is a factor leading to subsequent low vitality and eventual septic death . . . most of the deaths occurring post partum."<sup>5</sup>

Puerperal hemorrhage may be ante partum, post fetal, or post placental (post partum). The mechanism and management of hemorrhage in the first three stages have been adequately explained and classified. This paper, in presenting for consideration the "fourth stage of labor," necessarily deals with postplacental hemorrhage, and proposes to help combat it by recognizing the first postplacental hour as a separate and distinct phase of the process of labor. By so recognizing that hour as a physiologic entity having its own normal pattern and subject to its own peculiar aberrations, it is hoped that the post-placental hour can be more intelligently and uniformly handled, especially by those who too often assume that the labor is over with the delivery of the placenta.

Labor, as it is now universally understood, refers to the three classic stages: (1) stage of effacement and dilatation of the cervix; (2) stage of expulsion of the fetus, and (3) stage of placental separation and expulsion. As defined by Beck,<sup>6</sup> labor is that "process by which the mature products of conception are separated and expelled from the maternal organism."

DeLee,<sup>7</sup> however, defines labor more broadly, as "a function of the female organism by which the product of conception is expelled from the uterus through the vagina to the outside world *and the regressive metamorphosis of the genitalia started*.\* The latter part of DeLee's definition is not incompatible with, and is, in fact, a step toward the recognition of a fourth stage in the epic process of parturition.

Williams<sup>8</sup> almost conceded the presence of a fourth stage of labor, when he stated that "from a practical point of view, the hour following the delivery of the placenta is just as important as the actual third stage. Indeed, these *two periods*\* may be said to be more dangerous to the mother than *the other stages of labor*,"\* as is reflected in the immediate danger due to hemorrhage and the more remote risk of puerperal infection, as a result of the management of the patient at this time. These complications may prove fatal, or necessitate prolonged convalescence, but fortunately are often preventable."

In a review of the literature, the first mention of the "fourth stage" that could be found was made by Leff,<sup>9</sup> who suggested that the interval between the

\*Italics mine.

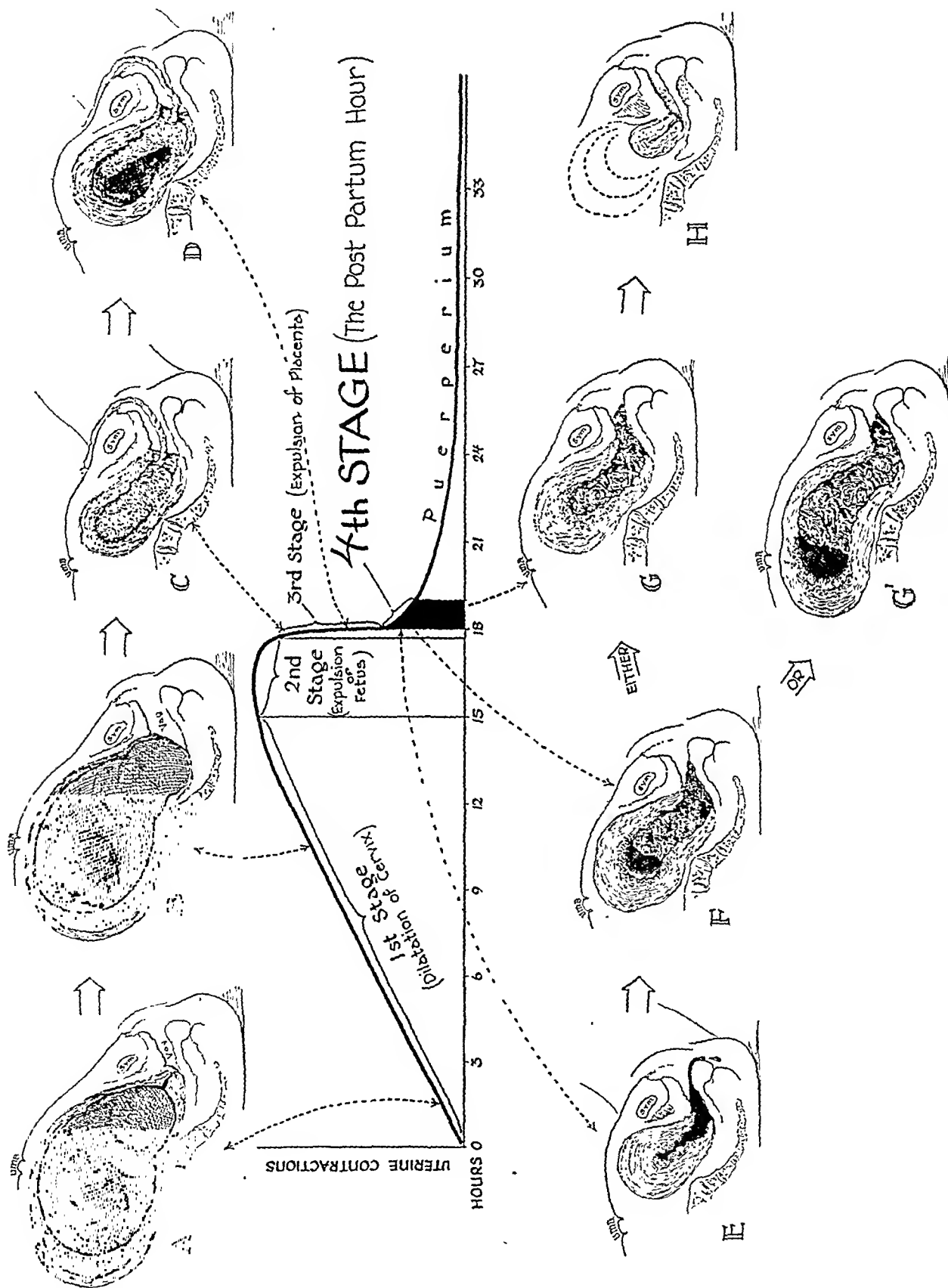


Fig. 1.—The stages of labor with special reference to the postpartum hour as the fourth stage of labor.



### Physiology of the Fourth Stage of Labor\*

The fourth stage represents the tapering off of the actual process of labor. (See Fig. 1.) It is the natural decrudescence of the process whose acme is attained with the expulsion of the products of conception, and whose increment is built up by many hours of contractions, which steadily mount in frequency and intensity. If the course of labor were graphically charted and compared with a graphic representation of the labor pain itself, it would be seen that the whole process of labor resembles each of its individual components, in sharing with them the characteristics of a gradual increment, a sustained acme, and a rapid decrudescence.

The normal fourth stage of labor consists of two main parts: (1) the contractile phase, and (2) the hemorrhagic phase. Both phases are, of course, inter-related and inseparable, but for purposes of lucidity will be described separately.

#### Contractile Phase

- A. Stage of *uterine myotamponade* (immediate uterine contraction).
- B. Stage of *uterine thrombotamponade* (secondary relaxation with formation of placental site sinusoidal and intrauterine hematomas).
- C. Stage of *myouterine indifference*.
- D. Stage of *fixed myouterine contraction*.

A. *Myotamponade*.—Immediately after the fetus is expelled, the uterus contracts and decreases in size; as the placenta separates, the uterus rises slightly and becomes more globular (Calkins),<sup>11</sup> only to further decrease in size after the delivery of the placenta; the uterus then usually contracts down to a point halfway between the pubis and umbilicus. Sometimes it descends to an even lower level, especially in a primipara under the influence of oxytocics. However, in multiparas, or even in primiparas under deep anesthesia, the immediate contraction stage may be very transitory, and the uterus (which is now usually slightly dextroverted) may rise to the umbilicus, or even above, shortly after placental delivery.

In the stage of immediate uterine contraction, tamponade is achieved by the compression, kinking, and twisting of the uterine vessels which are enmeshed in the multiplaned divagations of the myometrial whorls. *This is the first line of defense against postpartum hemorrhage.*

B. *Thrombotamponade*.—Thrombotamponade of the postpartum uterus depends upon (1) the thrombi in the large uteroplacental blood vessels, and (2) the intrauterine hematoma or hematomas with which the placental-site vessels may or may not be continuous. In the words of Teacher,<sup>12</sup> "the interior of the uterus in the first place is occupied by a thick mass of blood clot. This is easily stripped from the decidua vera but is more adherent at the placental site, as the clots are continuous with the thrombi in the torn ends of the large uteroplacental blood vessels."

The clot that begins to form in the cavity of the uterus after the placenta is expelled partially or completely fills the uterus as it gradually relaxes and rises again. After a gradual rise at the end of one hour, the uterus is at, or slightly above or below, the level of the umbilicus. The tamponading hematoma of the postplacental period, which is as important a mass to the fourth stage of labor as the placenta is to the third, is the *second line of defense against hemorrhage* in the early postplacental period when the sinuses of the placental

\*The functional processes of the postplacental hour, as are here postulated, represent the natural series of postpartum uterine events unmodified by oxytocics or other drugs, unless otherwise specified.

delivery of the placenta and the time the mother is put to bed in her room be known as the "fourth stage of labor." However, the interval between the delivery of the placenta and the time the mother is put to bed in her room is too variable to be used as a time ordinate against which to plot vital physiologic events. Furthermore a "norm" for the average fourth stage will have to be arrived at after a study of thousands of cases, just as "norms" have been ascertained for the average first, second, and third stages of labor in primiparas and multiparas. I propose that the first hour following the delivery of the placenta be considered as the normal duration of the fourth stage of labor, until further exhaustive studies will either add or detract a few minutes from the already rather arbitrarily accepted "postpartum hour."

With the average physician, in the average delivery room, the hour immediately following the delivery of the placenta has belonged neither to labor nor to the puerperium. It is the time when the patient, often in the throes of postanesthetic retching and vomiting, is stripped of the bloody drapes and transported to a stretcher amidst the nervous bustle of impatient nurses whose one thought is to get the patient off the table and into her room. Thus, an overconfident nurse who is ignorant of the physiology of the postplacental period and, therefore, its proper management, is a threat to the safety of the mother, especially when the postplacental hour is exclusively entrusted to her.

It is during this forgotten hour—this "no man's land" between labor and the puerperium—when most of the deaths caused by obstetric hemorrhage take place. These deaths occur because of the blind faith placed in a few quick clot-expelling jabs at the uterus, and in a cubic centimeter of ergot or pituitary preparations. They also occur because there are no adequate facilities for immediate blood transfusion, or because recognition of the necessity for blood transfusion comes too late.

This, of course, is not the procedure followed in our best clinics and hospitals, but it is, unfortunately, the procedure followed in the great majority of the delivery rooms and private dwellings in this country today. Beecham,<sup>10</sup> from a study of postpartum hemorrhage in Philadelphia for the years 1931 to 1936, concluded that "methods employed in the treatment of postpartum hemorrhage were often haphazard and lacking in uniformity."

By recognizing the hectic postplacental hour for its physiologic singularity and clinical importance, and by including it as an important fourth entity alongside its three predecessors in the labor records, the obstetric attendant would be impressed with the fact that the delivery is not yet over with the expulsion of the placenta. The early postplacental danger period would thereby be converted from a haphazardly handled to a scientifically handled and dignified hour. Such recognition of the first postplacental hour as the "fourth stage of labor," with its incorporation as such into the clinical labor records, would protect the mother, render an obstetric lesson to medical students and nurses, and serve as a guide and a check on the obstetrician, who would have to record his observations during the fourth stage, just as he has had to record his observations on the previous three. "The fourth stage" would lend needed dignity to the treacherous first postplacental hour, and instil more respect for its chief complication, postplacental hemorrhage, which is so dreaded and mishandled in inexperienced hands.

process which we call labor, and which we have heretofore arbitrarily consigned to the period up to and including the delivery of the placenta, but not beyond.

The fourth stage of labor varies in character with the parity of the mother and with the length and quality of the previous three stages. The greater the parity, the greater the tendency to a weakly contracting, vacillating, or "indifferent" uterus. Thus, the administration of small amounts of posterior obstetric pituitary extract to a cephalopelvically proportioned multipara whose cervix is fully dilated and who is having weak pains five minutes or more apart, may serve to tone the uterus and prevent postplacental hemorrhage due to uterine "indifference." The more protracted the first three stages, the greater the tendency to uterine muscle exhaustion and resulting atony and hemorrhage. If, on the contrary, the labor has been of very brief duration, there is likewise an added danger of postplacental hemorrhage (the exact reason for this is unknown). Polyhydramnios, multiple pregnancy, and large fetus, by excessive distention of the uterus, also predispose to a bleeding fourth stage. Peekham and Kuder<sup>13</sup> have reported a higher incidence of postpartum hemorrhage in primiparas than in multiparas, but the same authors state that the incidence of postpartum hemorrhage is greater in operative than in spontaneous deliveries, and the higher incidence of operative deliveries in primiparas may account for the higher rate of primiparous postpartum hemorrhage in their series.

A weakly contracting and "indifferent" uterus may perhaps be compared with a heart decompensating because of myocardial weakness. Thus, a uterus which is deficient in elastic tissue<sup>14</sup> (such as a multiparous uterus might be prone to manifest as part of the aging process), and perhaps stretched, thinned, hyalinized, and fibrosed by previous labors and arteriosclerosis, and its powers of contractility thereby weakened, may be considered the analogue of a dilated heart. When a dilated heart has reached the limits of its contractility, the blood dams back, as it is not adequately propelled forward; when a "dilated" uterus has reached the limits of its contractility, the uterine contents (fetus and placenta) remain a longer time (uterine atony), and, once expelled, the second mass of uterine contents (caval hematoma) is allowed to expand and grow by bleeding within the confines of its own yielding walls. The uterus may then contract and expel blood clots, either under the influence of injected oxytocic, spontaneously by its own strength, or by manual expression; only, however, to frequently relax again, and to again distend with blood. If this vacillating process repeats itself often enough, the patient may exsanguinate herself. This exsanguinating process is aided by intermittent well-intentioned but overzealous, deep, manual abdominouterine massage.

It is perhaps as unphysiologic to express blood clots from the uterus as it is to blow one's nose during a nosebleed. The clot that forms in the nose of the street urchin is sometimes treated with greater respect than the caval hematoma in the uterus of the postpartum mother.

*D. Fixed Myouterine Contraction.*—The safe attitude is to assume that the uterus has never quite reached a state of fixed contraction for ten days, for cases of delayed postpartum hemorrhage have been reported up to ten days or more. However, the late hemorrhages are usually due to retained secundines, or to the bleeding sites of partial or focal placenta accreta.<sup>15</sup> Many cases of so-called "delayed postpartum hemorrhage" within a few hours post partum, are not delayed hemorrhages at all, but hemorrhages whose recognition is delayed.

In a normal fourth stage, the uterus should be firmly and irreversibly contracted by the end of the first postplacental hour. Many uteri will achieve fixed contraction in less time, especially the primiparous and secundiparous ones; some will require a little more time and yet be within the range of normalcy. The upper limit, as Williams suggested, might perhaps be an hour and a half.

site are but freshly thrombosed, and the stage of fixed contraction has not yet been reached. The myometrial contractibility on the one hand, and the stimulation by the pressure of the clot on the other, finally attain a state of equilibrium, which may be called, "myothrombal equilibrium."

It is of the utmost importance to recognize the function of the single intrauterine hematoma or the continuous multiple hematomas as nature's tampon which, together with the contraction, retraction, and kinking of the uterine muscle fibers, cut off uterine hemorrhage by a simple pressure mechanism. In cases of strong and prolonged muscle contraction, there may be little or no caval clot. But in cases of mild contraction due to atony, the caval clot is of great importance, and its integrity must not be insulted by uterine squeezing which results in its partial or complete expression.

An excessively large placental site or the presence of the placental site in the passive lower uterine segment may be factors in inefficient uterine autothrombotamponade and myotamponade. In placenta previa, the fourth stage is therefore rife with greater risk, owing to the failure of adequate placental site contraction. In some hospitals, therefore, it is a rule to pack the uterus routinely after a placenta previa or marginalis delivery, as a prophylactic against hemorrhage.

*C. Myouterine Indifference.*—After expulsion of the placenta and subsequent autotamponade of the uterus, it would be a safe attitude to consider the uterus to be indifferent or apathetic from the contractile standpoint, for at least one hour; that is, it will remain in a state of isotonicity, hypotonicity, or hypertonicity, and may indeed transiently alternate between the three.

If there be frequent brisk massage with expression of clots and resulting temporary contraction (but often secondary relaxation), the stage of uterine indifference is prolonged; for the uterus will contract with each stimulation, and very often relax again when stimulation is ceased, to a point of isotonicity and then possibly hypotonicity, without the benefit of the myothrombal check because the clots have been expelled. For this reason, obstetricians who prefer to "squeeze the uterus dry," often order a tight binder over a suprapundal sandbag to control a fundus which was artificially overstimulated by hand and by injected oxytocin, and which was not permitted to achieve its own level. If, within certain limits, the uterus were permitted to rise and fill with clot, then heavy sandbags and tight binders would be unnecessary, and the unpredictable indifferent stage would be greatly shortened. Even when the uterus relaxes and rises, some degree of vascular compression still prevails, as the uterus rarely rises as high post partum as its height was before expulsion of the fetus.

The indifferent or apathetic uterus, even when undisturbed and permitted to fill with blood clot, may yet follow the alternating phases of contraction and relaxation with alternate expression of and refilling with clots; this is especially true when the patient coughs or vomits, or is jarred as in the movement from the delivery table to the stretcher cart, and from the cart to the bed. The obstetrician has no way of determining the final course which the typically vacillating postpartum uterus will take. Knowing the character of the fourth stage in the patient's previous labors might be of help. Guided by that information, if available, the obstetrician has but to gently palpate and stimulate the uterus with a force just below that which is required for the expression of clots, to watch, wait, and observe.

It would appear that it is unreasonable to expect a freshly emptied uterus to contract and remain contracted after hours of alternate contractions and relaxations. The alternating cycles of contractions and relaxations extending into the postplacental period and beyond, and often perceived by the patient as "after-pains," are the physiologic analogues of the labor pain itself, and are responses to the same unknown stimulus; they are a tapering off of the cyclically expulsive

The normal postpartum hemorrhage of the "nonclotting component" may, in some respects, therefore, be considered as a kind of first, acute, menorrhagic menstrual period.

### Comment

This presentation of the physiology of the fourth stage of labor is not offered in the fixed definitive sense; it is offered rather as a basis for further physiologic and pathologic research which will undoubtedly result in modifications of the present concept of the fourth stage of labor, especially in the present incomplete understanding of its polyhormonal control, and in its hematologic, histologic, and chemical ramifications.

Further physiologic investigation will probably show that two factors are in constant interplay in the contractile phase of labor, and that these two factors are as important in the fourth stage as in the initiation of the process of labor itself. These two factors are the contractogenic transmitters, which are probably hormones, of which the pituitary factor may be but one; and the contractile receptors, which are the muscle fibers, or special groups or bundles of muscle fibers arranged, perhaps, in a heretofore unrecognized myoneural conduction pattern as in the Pacemaker and Purkinje System of the heart. Pathology of either transmitter or receptor, or of a distant chemihormonal, local histopathologic, or intrinsic chemical block between the two would, in such a system, result in a failure to achieve normal, efficient, uterine contraction.

The anticlottting enzyme<sup>17</sup> of the uterus (which, if it exists, I propose it be called "hysterin") or the lack of or the neutralization of a certain clotting component, may explain the failure of a component of postpartum blood to clot. This nonclotting component may be the explanation for a nonclotting type of postpartum hemorrhage,<sup>18</sup> whose true basis may have erroneously been relegated to the category of "shock bleeding." The possibility of the existence of the latter mechanism in certain cases of postpartum hemorrhage, either alone or superimposed, is not denied, however.

Postpartum hemorrhage, when not due to uterovaginal tract trauma, may consist of a hemorrhage of (a) one of the clotting components, (b) the non-clotting component, or (c) a combination of any two, or all three.

### Summary

1. A tapering-off of the process of parturition occurs during the post-placental hour; this decrease should be recognized as the "fourth stage of labor."
2. The fourth stage of labor is a physiologic and clinical entity.
3. The physiology of the fourth stage of labor is postulated, the two main physiologic phases being:

#### I. *The Contractile Phase*

- A. Stage of "*Uterine myotamponade*"  
(immediate uterine contraction).
- B. Stage of "*uterine thrombotamponade*"  
(secondary relaxation with formation of placental site sinusoidal and intrauterine hematomas).
- C. Stage of "*Myouterine indifference*."
- D. Stage of "*Fixed myouterine contraction*."

Should the uterus continue to alternately contract and relax, or should the uterus undergo acute passive dilatation, then the fourth stage should be considered delayed and abnormal, and even more carefully followed. Failure to achieve the state of fixed contraction results in hemorrhage, or the immediate possibility of hemorrhage. The hemorrhage may be overt or concealed. When concealed, the hemorrhage is in the form of a caval hematoma which is tamponading; and, though it may gradually grow in size, it would be exsanguinating only if repeatedly expressed through the vagina, or lacking that outlet, if it escapes through the rent of a previously ruptured uterus.

### Hemorrhagic Phase

The normal hemorrhagic phase of the fourth stage of labor concerns itself with two main types of physiologic hemorrhage, traumatic and atonic:

#### A. Traumatic Hemorrhage

1. Uterovaginal tract laceration bleeding (Component One)

#### B. Atonic Hemorrhage

1. The clotting hemorrhagic component (Component Two)
2. The nonclotting hemorrhagic component<sup>16</sup> (Component Three)

*The Components of Normal Postpartum Hemorrhage.—Component One:* Traumatic hemorrhage of the mild variety is physiologic. If a test tube be inserted into the vagina (above the episiotomy, if there be any) immediately after fetal but before placental delivery, a few cubic centimeters of clotting blood can almost always be collected; this is due to uterocervical-vaginal trauma.

*Component Two:* The next collectable blood sample is that hemorrhage associated with placental separation, and which continues following the atonic rise of the uterus after placental delivery, but before the uteroplacental sinuses have begun to thrombose. This blood sample clots very quickly, either because of some factor it contains which promotes clotting, or because it has already begun to clot while a part of the retroplacental hematoma, or while it made its way in its meandering trickle down the pathway of the uterovaginal tract.

*Component Three:* (The nonclotting component.)<sup>16</sup>

Shortly after the delivery of the placenta is completed, the uterus, even after it is contracted by oxytocics and external stimulation, will continue to ooze a nonclotting blood, either spontaneously or upon manual transabdominal uterine compression. This "nonclotting component of normal postpartum blood" is collectable up to twenty-four or more hours post partum. The blood, when collected in a test tube, does not clot even if kept for days; when the test tube containing the cellular sediment is agitated, the cells are easily resuspended homogeneously. (In any of these samples, especially the early ones, there may be present a small contaminatory clot from one of the antecedent clotting components of postpartum blood.)

The "nonclotting component" probably comes from the bleeding myometrium recently denuded of its decidua. The clotting component, which is associated with placental separation, is normally shut off with the twisting, kinking, compression, and thrombosis of the placental site vessels during the stages of myotamponade and thrombotamponade.

This normal "nonclotting component" of postpartum blood may be analogous with the nonclotting component of menstrual blood which this author believes also consists of two components, a clotting and a nonclotting. The same uterine enzyme which may be responsible for the failure of one of the postpartum blood components to clot may be responsible for the failure of one of the menstrual components to clot.

# PATHOLOGIC FINDINGS IN GENITAL BLEEDING TWO OR MORE YEARS AFTER SPONTANEOUS CESSATION OF MENSTRUATION

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IN 1930, 157 cases of genital bleeding occurring on the Gynecological Service of the Johns Hopkins Hospital were studied from a clinico-pathologic viewpoint and reported by TeLinde.<sup>1</sup> He found malignancy to be the cause of the bleeding in 55.9 per cent. In 1937, he<sup>2</sup> augmented the series and reported on 349 cases, occurring on the service between Jan. 1, 1919, and Jan. 1, 1935. In the larger series he found the incidence of malignancy to be 53 per cent. The literature up to 1941 reveals an alarmingly high proportion of malignant to benign causes of the bleedings.

TABLE I

YEAR	AUTHOR	LOCALITY	NO. OF CASES	PER CENT MALIGNANCY
1930	TeLinde <sup>1</sup>	Johns Hopkins Hospital, Baltimore	157	55.9
1931	Ducuing <sup>3</sup>	Toulouse Cancer Clinic, France	326	90.0
1932	Kanter and Klawans <sup>4</sup>	Presbyterian and Cook County Hospital, Chicago	98	68.4
1933	Schultze <sup>5</sup>	University of California Hospital, San Francisco	315	68.0
1933	Geist and Matus <sup>6</sup>	Mt. Sinai Hospital, New York City	182	57.5
1935	Norris <sup>7</sup>	University of Pennsylvania, Philadelphia	189	53.0
1937	TeLinde <sup>2</sup>	Johns Hopkins Hospital, Baltimore	349	53.0
1938	Keene and Dunne <sup>8</sup>	University Hospital, Philadelphia	782	60.0
1938	Taylor and Millen <sup>9</sup>	Roosevelt Hospital, New York City	406	63.0
1941	Geiger <sup>10</sup>	Loyola and Cook County Hospital, Chicago	395	81.0

Within the past several years estrogens have been used and misused on a tremendous scale. Attention has been called to the misuse by Scheffey<sup>11</sup> and others. As a result, serious organic genital lesions are often prevented from being properly evaluated. In addition, much genital bleeding is artificially induced by the use of estrogens, particularly stilbestrol. Offsetting the effect of this enthusiasm for hormones, the medical journals have published many articles, warning the profession of the sinister significance of postmenopausal bleeding. In view of these cross currents of therapeutic hyperenthusiasm and public enlightenment, it seemed appropriate to restudy the cases of postmenopausal bleeding in our clinic.

This study was undertaken on 514 cases occurring on the private and public ward services and in the dispensary of the Johns Hopkins Hospital. In order



## II. *The Hemorrhagic Phase*

### A. *Traumatic hemorrhage*

1. Uterovaginal tract laceration bleeding. (Component One.)

### B. *Atonic Hemorrhage*

1. The clotting hemorrhagic component associated with placental separation. (Component Two.)
2. The nonclotting hemorrhagic component probably arising from denuded myometrium.<sup>16</sup> (Component Three.)

4. Both the contractile and hemorrhagic phases are simultaneous and inter-related.

5. The official recognition and physiologic appreciation of the fourth stage of labor would result in a reduction of mortality from postpartum hemorrhage, which is assuming first place among the causes of maternal mortality.

6. A questionnaire concerning the fourth stage of labor should be part of every labor record.

7. The normal "nonclotting component"<sup>16</sup> of postpartum blood may be analogous with the nonclotting component of menstrual blood which this author believes also consists of two components, a clotting and a nonclotting. The same uterine enzyme<sup>17</sup> which may be responsible for the failure of one of the postpartum blood components to clot may be responsible for the failure of one of the menstrual components to clot.

8. Postpartum hemorrhage, when not due to uterovaginal tract trauma, may consist of a hemorrhage of (a) one of the clotting components, (b) the non-clotting component, or (c) a combination of any two, or all three. "Shock bleeding"<sup>18</sup> may be a superimposed late complication.

The author wishes to thank Mr. Melford Diedrick of the Buffalo General Hospital for the illustration.

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Exceptions to the above were made as follows: (a) In cases of pyometra when curettage and biopsy were postponed until the pyometra had been drained by dilatation of the cervical canal. Two cases of pyometra subsequently found to have endometrial carcinoma received radical surgery without preliminary curettage. (b) In one case of suspected carcinoma of the endometrium pan-hysterectomy and removal of adnexa were performed without preliminary curettage. (c) Occasionally biopsy of the cervix was omitted in the private practice of visiting gynecologists if the cervix appeared normal. (d) Curettage of the uterine cavity was omitted in cases of definite epidermoid carcinoma of the cervix with necrosis and infection.

TABLE II. PATHOLOGIC FINDINGS ACCORDING TO LOCATION

<i>Vulva:</i>	Carcinoma	2	
	Melanosarcoma clitoris	1	
	Ulcer, nonspecific (not granuloma)	2	
<i>Urethra:</i>	Carcinoma	5	
	Caruncle	10	
	Prolapse	2	
	Urethritis	1	
<i>Vagina:</i>	Carcinoma	1	
	Vaginitis, senile	60	
	Granuloma inguinale	1	
	Trauma	5	
	Pessary	5	
<i>Cervix:</i>	Carcinoma	104	
	Polyp	37	
	Prolapse	35	
	Cervicitis marked	36	
<i>Uterus Corpus:</i>	Carcinoma	58	
	Sarcoma of endometrium	2	
	Sarcoma in myoma	2	
	Myoma, submucous	18	
	Polyp, endometrial	18	
	Hyperplasia of endometrium	20	
	Endometritis, pyometra	6	
<i>Tube:</i>	Carcinoma	1	
	Tuberculosis	1	
<i>Ovary:</i>	Malignancy		
	Papillary cystadenocarcinoma	3	
	Medullary carcinoma	1	9
	Krukenberg tumor	2	
	Granulosa-cell tumor	3	
	Benign		
	Papillary serous cystadenoma	1	
	Serous cystadenoma	1	4
	Pseudomucinous cystadenoma	2	
<i>Bleeding probably from estrogen therapy:</i>			12
<i>Unknown cause, including seven with probable recrudescence of ovarian function:</i>			56
			<hr/> 514

Since any bleeding from the female genitals was included in this study, lesions of the vulva and urethra are found in the tabulations. There were a number of cases in which the bleeding on initial physical examination was thought to come from atrophic vaginitis, a caruncle, or cervical erosion, but on complete study was found to issue from carcinoma of the cervix or a lesion higher in the tract. The point cannot be too strongly emphasized that costly mistakes will occur if one jumps to the conclusion that easily detected superficial lesions are responsible for the bleeding.

to obtain as nearly as possible a real cross-section impression of postmenopausal bleeding occurring in the Clinie, women referred for treatment for previously proved carcinomas were excluded from this study. The distortion in incidence which would arise from including such cases is illustrated by the report in Table I from the Toulouse Cancer Clinie, where 90 per cent of the cases of postmenopausal bleeding were found due to cancer. A comparison of this figure, with the statistics from other clinics, clearly indicates that it does not represent the incidence of malignancy on a general gynecologic service.

In surveying the literature, it is apparent that there is much difference of opinion as to just what constitutes the postmenopausal period. TeLinde limited his cases to those in which there was a reappearance of bleeding after a year of amenorrhea. Most authors fail to mention their time limit. In this study we have made an arbitrary limit of two years' amenorrhea. Since this limit would rule out many cases of benign bleeding shortly after the cessation of the normal menses, it should increase the incidence of malignancy.

### Material

There were 514 cases, occurring over a period of seven and one-half years, which have met the two requirements:

1. Initial pathologic diagnosis must have been made in the Department of Gynecological Pathology.
2. At least two years must have elapsed before genital bleeding recommenced.

These cases were collected in the following manner:

1. The operation files were scanned for patients whose tentative operative diagnosis was "postmenopausal bleeding." The names of all women 45 years old or over were noted and the hospital or office records studied for menstrual data. Among 13,959 operations, 402 were performed on women who had postmenopausal bleeding, representing 3.3 per cent.

2. The records of the Department of Gynecological Pathology were examined for menstrual data. The remaining 52 cases of this series were obtained from this source and represent cases which were either too far advanced to have reached the operating room for application of radium, or were referred elsewhere for treatment. In the seven-and-a-half year period covered by study, a total of 16,742 pathologic case reports were reviewed.

3. A single cause for the bleeding was determined in each case from a combined study of the history, and clinical and pathologic reports. Multiple causes were avoided, and in borderline cases the history and material were reviewed again for final decision.

4. With few exceptions the patients received a complete diagnostic study which included the following: (a) general physical examination. (b) gynecologic examination with visualization of the cervix and vagina, and pelvic bimanual palpation. (c) digital examination of the anus and rectum; proctoscopy, if indicated. (d) Examination of catheterized urine. If there were urinary symptoms and persistent abnormal microscopic findings, cystoscopy, catheterization of the ureters, differential phthalein, and retrograde pyelography were carried out. (e) Routine hemoglobin and white blood cell count. Complete blood study was done if there was an unexplained anemia. (f) Biopsy of the cervix regardless of its appearance. (g) Curettage of the cervical canal and uterine cavity.

*Tube.*—Primary carcinoma of the tube, a rare disease, occurs once in this series. A 58-year-old woman began vaginal bleeding eleven years after the menopause. The bimanual examination was thought to reveal nothing in the adnexal regions. On curettage, atrophic endometrium was obtained. Bleeding continued for six weeks. Another curettage was done. At the time of this operation a mass was felt in the left adnexal region. Because of the patient's age, the continued bleeding and the presence of an adnexal mass not previously observed; the operator, thinking that there was an ovarian tumor, performed a laparotomy, removing the entire uterus and adnexa. The left tube was swollen and, on microscopic study, was found to contain adenocarcinoma. Bleeding in this case must have come from the tube. Careful re-examination of the curettings revealed no suspicious cells.

In the single case of tuberculous salpingitis, a colored woman 59 years of age began having leucorrhea and slight vaginal bleeding after fifteen years of amenorrhea. A curettage after two years of spotting yielded insufficient endometrium for diagnosis and the cervix was atrophic. She died several months later, and at autopsy was found to have tuberculosis of the right Fallopian tube. This was the only apparent cause of the bleeding.

*Ovary.*—Tumors of the ovary, malignant and benign, were associated with genital bleeding in 13 cases. In the nine patients who had malignant tumors there were six who had extension of the carcinoma to the tube or uterus, probably accounting for the hemorrhage. An endocrine cause of bleeding may be postulated in the three granulosa-cell tumors. Of the four benign tumors, the cause is obscure, although one had an endometrial polyp which may have caused the bleeding.

*Estrogen Therapy.*—There are twelve women in the series who had received some form of estrogen which is considered a probable factor in the postmenopausal bleeding. Stilbestrol had been given to seven, amniotin, estrone or theelin to four, and in one case the medication is not stated. Curettings in two of the stilbestrol group showed the histologic picture of benign hyperplasia. One woman who was given an implantation of 50 mg. of estrone subcutaneously four years after her last period, bled one month later. Curettings showed secretory glands, and the tissue had the appearance of menstruating endometrium. It cannot be proved or disproved whether the estrone was a factor in the bleeding, but the secretory endometrium must signify some corpus luteum activity in her ovary. For the most part, in these hormonal therapy cases there was relatively little endometrium obtained.

It is our practice to carry out curettage in every case of abnormal bleeding following estrogen therapy. None of the 12 cases of this group was found to have carcinoma of the cervix or endometrium. This, however, is a small group, since relatively few women receive estrogen two or more years past the cessation of menstruation. During this survey, however, we noted several instances of carcinoma in estrogen-treated women whose period of amenorrhea was less than two years. We do not conclude from this that estrogen possesses carcinogenic powers, but rather that this was due to the ill-advised use of estrogen as a substitute for diagnostic curettage in abnormal bleeding before the patients reached the hospital.

*Bleeding of Unknown Etiology.*—In 56 cases (10.9 per cent) no satisfactory pathologic explanation of the bleeding was found. In six cases it is believed that a recrudescence of ovarian function may have been a factor. Except for one of these, whose endometrium showed secretory activity, this impression is based solely on the history of recurrent bleeding. The endometrium of the others was scanty in amount. In trying to establish the source of bleeding, it must be remembered that pedunculated submucous myomas and polyps of the endometrium may be missed on curettage. It is quite possible that some of

In Table II certain points are worthy of more detailed comment.

*Vulva.*—The bleeding from a nonspecific ulcer occurred in a white woman who was suffering from pruritis. The blood Wassermann was negative and a curettage revealed no other cause for bleeding. The remaining cases need no comment.

*Urethra.*—The case with urethritis had definite bleeding from a urethra which seemed not to be prolapsed and did not have a caruncle. Biopsy of the granular mucosa confirmed the clinical impression.

*Vagina.*—Atrophic vaginitis is indicated as a cause of bleeding when there was obvious bleeding from a thin, smooth vaginal mucous membrane, and when curettage of the cervical canal and uterine cavity revealed no other possible source of the bleeding. The presence of bleeding from an atrophic vaginal mucous membrane is not considered a license for omission of curettage and biopsy of the cervix. The woman with granuloma inguinale was bleeding profusely from a vaginal extension of the process. There are only five cases in this series where the bleeding was attributable to vaginal irritation from a pessary. There were three women who bled as a result of hot douches, and one who said she had "fallen off a hayrick." All of these had atrophic vaginitis which had caused no trouble until traumatized. The woman with the retained suture had had a vaginal plastic operation elsewhere one year previously. Bleeding stopped after the black silk suture was removed.

*Cervix Uteri.*—Prolapse of the cervix is listed as a cause when there was an ectropion of the endocervical mucosa or a decubitus ulcer bleeding on examination. These lesions should always be biopsied, for there were three cases in which cervical carcinoma occurred in a prolapsed cervix. Chronic cervicitis is not commonly recognized as a cause for bleeding. In this series, however, 36 cases were encountered in which blood was seen coming from the cervical portio, and no other source could be found on complete examination.

*Corpus Uteri.*—Hyperplasia of the endometrium is listed here among causes of postmenopausal bleeding and there were 20 such cases. Bleeding for the most part had been scanty and intermittent. The actual source of the bleeding is not easily evaluated, although four of the 20 had definite small endometrial polyps, and ulceration of the surface epithelium may have been a factor. The immediate cause of bleeding is not established in the other cases. In 13 of the 20 cases there had been more than four years of amenorrhea before hemorrhage recommenced. The average age at the time of bleeding was 54 years. The oldest was 67, the youngest 42 years. There are six who were over 60 years of age.

In 18 cases bleeding is ascribed to endometrial polyps. Two of these were associated with benign hyperplasia but were not included in that group because the polyps were large and grossly showed bleeding ulcerated surfaces.

Marked chronic or subacute endometritis was found in the curettings from six women who had no other source of bleeding. Of these there were four who had gross pyometra, and hence only an initial dilatation of the cervix was done, followed later by curettage when the discharge had subsided. There are five cases of endometrial carcinoma associated with pyometra which are not included here because of the more significant causal lesion.

Submucous myoma's caused postmenopausal bleeding in 18 cases. In two of these there was extrusion of the myoma through the cervix, and one of these had had a similar submucous myoma removed vaginally four years earlier, two years before her menopause. In this group of 18 cases only one of the women had had menorrhagia or metrorrhagia toward the close of her menstrual life. This finding is in accordance with the point brought out in 1940 by TeLinde<sup>12</sup> that some myomas may become submucous during involution of the uterus after the menopause. In some of our cases this apparently occurred after the age of 60 years.

In sharp contrast to this middle group is the small group of women who stopped menstruating earlier than 40 or later than 55 years of age. There are only six who stopped before they were 35, but, of these, four (67 per cent) had malignancy. None had had an operation that might have brought on a premature menopause. Carcinoma of the endometrium occurred 12 times (60 per cent), compared to only eight benign causes. One of these had carcinoma of the urethra, another a granulosa-cell tumor of the ovary with liver metastases, six cervical carcinoma, two endometrial carcinoma, and one had sarcomatous degeneration of a myoma. Of 37 women who stopped menstruation after the age of 55 years, there are 18 (49 per cent) who had malignancy. These consist of one carcinoma of the endometrium, one sarcoma of unknown etiology in the pelvis, 12 cervical, and four endometrial carcinomas.

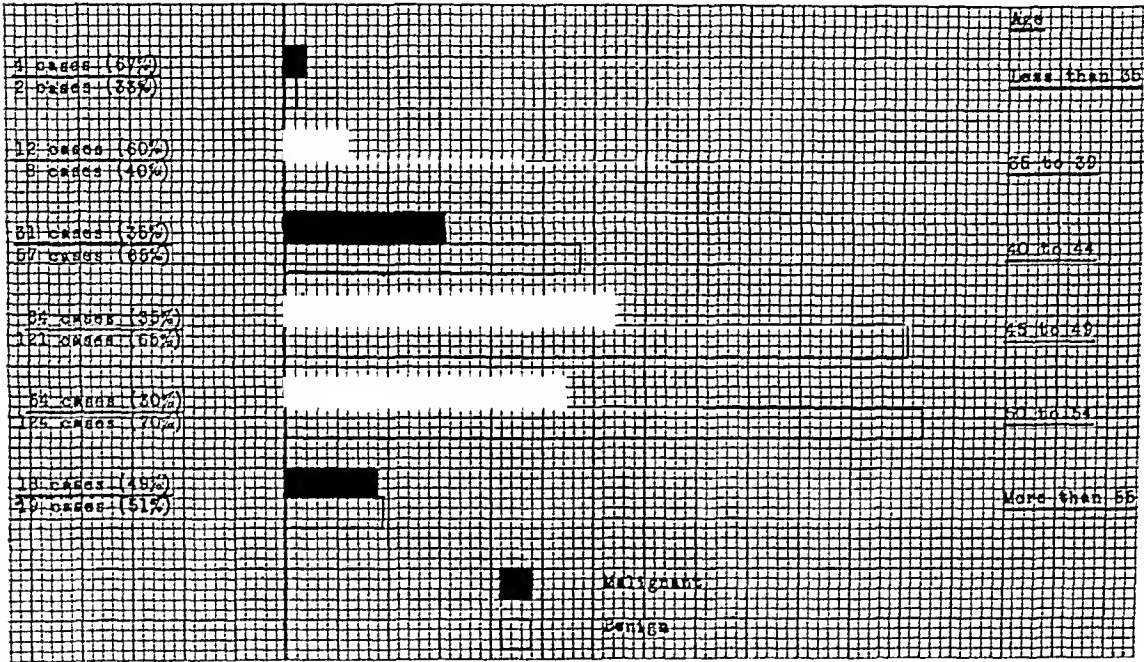


Fig. 1.—Proportion of malignancy according to age at the time the menopause occurred.

The question at once arises as to whether or not this varying proportion of malignancy to nonmalignancy according to age at the menopause is more apparent than real. It is to be expected that with increasing age there would be an increasing proportion of malignant to benign lesions, and this seems true when the ages at the time of diagnostic operation are tabulated in groups of five-year periods.

*Duration of Amenorrhea Before Bleeding.*—The length of time elapsing between menopause and onset of genital bleeding varies from two years, arbi-

TABLE IV. AGE AT CURETTAGE

	LESS THAN 50	50-55	55-60	60-65	65-70	MORE THAN 70
Malignant	13 (30%)	28 (26%)	48 (40%)	36 (40%)	33 (45%)	24 (53%)
Benign	30 (70%)	79 (64%)	71 (60%)	54 (60%)	40 (55%)	21 (47%)

the 56 cases where bleeding was unexplained might have had small submucous myomas or polyps, since only one of the group had a hysterectomy.

Since hypertension is occasionally mentioned in discussion of abnormal bleeding, the blood pressures of individuals whose bleeding is unexplained were compared with those of groups with submucous myomas, polyps, and endometrial hyperplasia. No appreciable difference could be found. The average pressure was 151/85. In the laboratory, during its fifty-two years of existence, we have not observed a single case of "uterine apoplexy" in a nonpregnant uterus. Any less obvious manifestation of hypertensive uterine bleeding would test a pathologist's credulity.

TABLE III. PROPORTION OF MALIGNANT TO BENIGN LESIONS BY ORGANS

	TOTAL NUMBER	MALIGNANT	BENIGN
Vulva	5	3 (60%)	2 (40%)
Urethra	18	5 (27.8%)	13 (72.2%)
Vagina	72	1 (1.4%)	71 (98.6%)
Cervix	212	104 (49.1%)	108 (50.9%)
Corpus	124	62 (50%)	62 (50%)
Tube	2	1 (50%)	1 (50%)
Ovary	13	9 (69.2%)	4 (30.8%)
Estrogen therapy	12	0 (0%)	12 (100%)
Unknown	56	0 (0%)	56 (100%)
Total	514	185 (36.1%)	329 (63.9%)

### Discussion

*Race.*—In the group there were 154 (30 per cent) Negro and 360 (70 per cent) white patients. Bleeding from prolapse of the cervix occurred only three times in the Negro patients, as compared with the 32 white patients. This is commensurate with our experience that prolapse in Negro women is rare.

*Age at Menopause.*—The average age at the time of cessation of menstruation, used synonymously with "menopause" in this paper, was 47.8 years. Norris found 47.5 years the average age in 200 cases. There were 26 women, 5 per cent, whose periods stopped before the age of 40 years. Of these, 18 were white and eight were Negro. This is in proportion to the total number of white to Negro patients in the series. The earliest menopause occurred spontaneously at the age of 25 years in a white woman who began irregular bleeding at 44 years and was found to have adenocarcinoma of the corpus at 50 years of age.

Of the 25 patients with menopause before the age of 40 years, there were four who had undergone surgery previously. One had stopped menstruation after a simple cesarean section when she was 36 years of age. She bled from a submucous myoma nine years later. The other three had stopped two, nine, and seventeen years after partial or complete removal of an ovary.

There were 215 women, 42 per cent, who stopped menstruating after the age of 50 years. There were 37 (7 per cent) who were 55 years of age or older. The oldest patient at the menopause was a white woman 59 years of age.

*Relation of Age at Menopause to Cause of Postmenopausal Bleeding.*—Although the number of cases in each group is too small to justify a statistical conclusion, the figures suggest a curve pattern that warrants further evaluation. The cases are divided into groups according to the age at the time menstruation ceased. The majority, 451 (86 per cent) fall between 40 and 55 years. Malignancy was responsible for bleeding in 33 per cent of these cases.

7. Bleeding after the menopause may come from anywhere in the genital tract. To rule out malignancy a complete study, including uterine curettage and biopsy of the cervix, is imperative in all cases regardless of findings on pelvic examination.

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trarily set as the definitive minimum, to thirty-five years. No correlation is found between the length of amenorrhea and the cause of postmenopausal bleeding. The average duration of amenorrhea for the entire group is 10.1 years.

*Duration of Bleeding.*—Duration of postmenopausal bleeding gives no indication of the responsible lesion. Approximately 5 per cent bled for a week or less before operation. Another 5 per cent bled for ten years or longer. The shortest duration was one day; the longest, seventeen years.

TABLE V. TYPE OF BLEEDING WITH REFERENCE TO PATHOLOGIC LESION

	MALIGNANT	BENIGN	TOTAL
Rhythmical	6 (1.1%)	11 (2.1%)	17 (3.2%)
Profuse	75 (14.6%)	126 (24.4%)	201 (39%)
Spotting	78 (15.1%)	147 (28.5%)	225 (43.6%)
Bloody discharge	26 (5.5%)	45 (8.7%)	71 (14.2%)
Totals	185 (36%)	329 (64%)	514 (100%)

### Summary

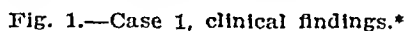
1. A brief review of the literature is presented.
2. A survey is made of 514 cases of genital bleeding two or more years after cessation of menstruation.
3. Criteria are reviewed with respect to: (a) pathologic findings according to location, (b) race, (c) age at menopause, (d) duration of amenorrhea before bleeding, (e) duration of bleeding, (f) type of bleeding.
4. Explanatory comments are made concerning some of the more interesting cases.

### Conclusions

1. Of the 514 cases presented, 36.1 per cent had malignant lesions. This is a lower figure than that usually quoted, and reflects increasing understanding on the part of the patient of the danger of postmenopausal bleeding, better understanding and cooperation on the part of attending physicians in referring patients for study, and possibly a greater incidence of benign bleeding from hormonal stimulation.
2. No significant difference in etiology is noted when the group is divided according to race, except that cervical prolapse associated with bleeding was uncommon in the Negro race.
3. The average age of cessation of menstruation was 47.8 years. In the groups divided according to age at the menopause, there is apparently no real difference in percentage of malignancy. There is an increasing percentage of malignancy with increasing age of the patient at the time of examination.
4. There is no relation of duration of amenorrhea to the causal lesion. The average of 10.1 is higher than expected.
5. Duration of bleeding ranges from one day to seventeen years and bears no relation to pathology.
6. Type of bleeding varies from spotting to profuse hemorrhage and is found to have no significance in determining the etiology.



Two weeks later the patient was readmitted in labor. The blood pressure at this time was 145/80, and all other findings were otherwise normal. Delivery of a 3,570 Gm. normal female infant was spontaneous after twelve and three-fifths hours of uneventful labor. During the first six postpartum days the blood pressure was normal to borderline, with varying minimal proteinuria.



In the following eight days the elevated systolic blood pressure fluctuated widely, although the diastolic pressure was maintained at about 90. During the remainder of the hospital stay the blood pressure was within normal limits.

\*The average systolic pressure during a given period is indicated by the solid line. The dotted lines indicate the highest recorded pressure which occurred.

## LATE POSTPARTUM ECLAMPSIA\*

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POSTPARTUM eclampsia occurs most frequently during the first day of the puerperium, while in only a relatively small number of cases does the attack appear on the second day after the birth of the child. It is generally stated that convulsions appearing later in the puerperium are due to such causes as hysteria, epilepsy, or uremia rather than eclampsia. A few instances have been reported in which convulsions occurred several weeks after delivery, but the evidence presented with these reports is insufficient to substantiate the diagnosis of postpartum eclampsia.

Until recently, our experience has led to the conclusion that postpartum eclampsia invariably occurs within seventy-two hours following parturition. In light of the data presented below, this belief becomes untenable and must be altered to include the first week of the puerperium.

TABLE I. POSTPARTUM ECLAMPTICS. TIME OF FIRST CONVULSION

HOURS FOLLOWING DELIVERY	NUMBER OF CASES	PER CENT OF TOTAL	SUM OF PERCENTAGE
0 to 6	12	50	50
6 to 12	4	17	67
12 to 24	4	17	84
24 to 30	1	4	88
Over 30	3	12	100
Total	24	100	

In the New York Lying-In Hospital, during the period from Sept. 1, 1932, to Jan. 1, 1946, we have had 70 cases of eclampsia of all types, an incidence of one in every 547 premature and full-term deliveries. Of these eclamptic patients, 24, or 34 per cent, suffered from the postpartum variety. An analysis of these (Table I) shows that the first convulsion occurred within thirty hours of delivery in 21 cases. In other words, the attack of postpartum eclampsia came on well within the seventy-two hours following parturition in 88 per cent of women suffering from this variety of the disease. There remain three cases, detailed in this paper, in which the eclamptic seizure made its appearance after this seventy-two hour period, one occurring on the fourth, one on the sixth, and one on the eighth postpartum day. A summary of the pertinent findings in these three patients follows.

CASE 1.—Mrs. M., a 31-year-old primigravida, registered in the antenatal clinic in the seventeenth week of her pregnancy. Her past history was relevant in that during the preceding four years she had had episodes of hyper-

\*Supported by a grant from The John and Mary R. Markle Foundation.

infant and a 2,180 Gm. living female infant were delivered by low foreeps and by breech extraction, respectively. The blood pressure on admission was 155/90, but dropped to normal later in labor.

The first three days following delivery were uncomplicated. At 11:15 A.M. on the fourth postpartum day, the patient was seized with generalized convulsions, preceded by visual disturbances described as "spots before the eyes." Within six hours she had three additional convulsive attacks. She was unconscious after each attack. The blood pressure at the time of the first convulsion was 140/90, rising to 200/76 with the second seizure. The optic fundi were visualized and found normal. Blood taken at the time of the first episode revealed a uric acid of 3.9 and a CO<sub>2</sub> combining power of 29.6 volumes per cent. Within a few hours the uric acid had increased to 4.9, but under treatment the CO<sub>2</sub> combining power returned to normal. The urine contained three plus albuminuria. The patient was given sedation, and the blood pressure slowly returned to normal over the course of the next two weeks. Likewise, the blood chemical changes had returned to normal in thirteen days.

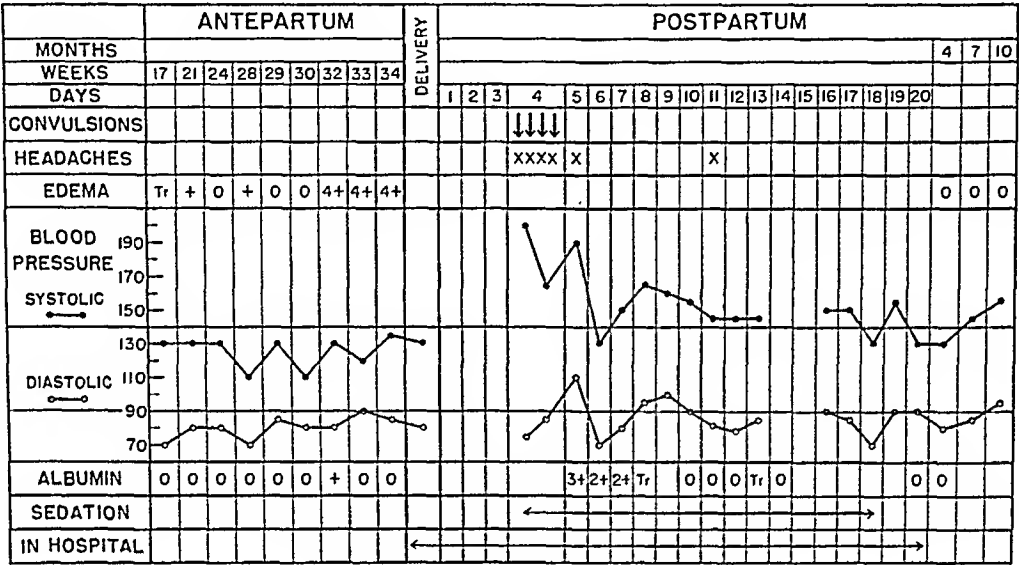


Fig. 3.—Case 2, clinical findings.

Proteinuria persisted for four days. Lumbar puncture on the day of convulsions revealed an initial pressure of 180, dropping to 120 mm. later; microscopic and chemical determinations were normal. Skull x-rays were normal. There was no past history of convulsions, save for one attack in infancy. Her course was afebrile save for a single temperature rise to 38.8° C. (rectal) following the convulsive seizures. She was discharged in good condition on the twenty-first postpartum day.

The patient was seen in the postpartum toxemia clinic at stated intervals, and was last observed ten months post partum. She had no complaints, and the only abnormal finding was a final blood pressure of 155/95, as shown in Fig. 3. Diagnosis: Postpartum eclampsia.

CASE 3.—Mrs. M., a 25-year-old white para 0, gravida ii, registered in the antenatal clinic in the eighteenth week of pregnancy. Her past history was negative. Physical examination was normal with normal blood pressure. A Wassermann test was negative, the blood was type A and Rh negative. Her antepartum course was uneventful until the beginning of the thirtieth week, when the diastolic blood pressure became elevated. Both systolic and diastolic

Likewise, there was a gradual return to normal values in the blood chemistries. The urine output was satisfactory throughout and contained only a trace of proteins. A urea clearance test on the twentieth postpartum day showed a clearance of 116 per cent of normal. Retinoscopic examination following the convulsion was negative. A lumbar puncture on the third day following the convulsion revealed normal pressure, clear fluid, and negative microscopic findings. Protein was 75 mg. per cent. She was discharged in good condition on the twenty-first postpartum day.

The patient was followed at stated intervals in the postpartum toxemia clinic for two years and eight months. Her only complaints were occasional precordial pains. There was no proteinuria and no edema. The blood pressure, however, showed a progressive rise in systolic to 180, but with a maintenance in the diastolic at 90. Diagnosis: postpartum eclampsia in a patient with essential hypertension. Blood pressure readings, urine and blood chemical findings, and other pertinent data are portrayed in Figs. 1 and 2.

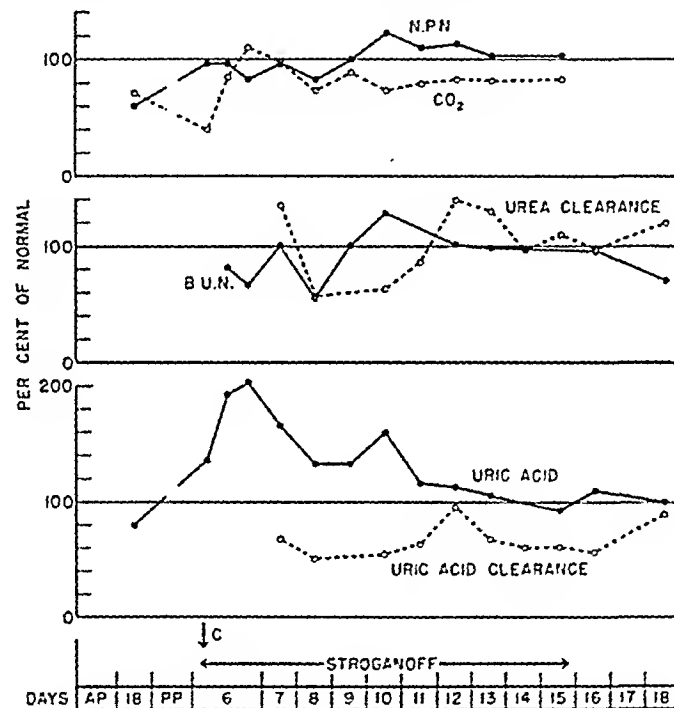


Fig. 2.—Case 1, laboratory findings in blood and urine.\*

CASE 2.—Mrs. T., aged 42 years, an elderly primigravida, registered in the antenatal clinic in the seventeenth week of her pregnancy. Her past history was negative. The physical examination at this time was normal, including normal blood pressure values and normal pelvic measurements. Her antepartum course was uncomplicated, except for a slight anemia, until in the thirty-second week, when a one plus proteinuria appeared associated with a four plus edema, blood pressure being normal. One week later the urine was negative for albumin, the edema was unchanged, and the blood pressure was 120/90. In the thirty-fourth week the blood pressure was 140/88. Multiple pregnancy (twins) had been recognized since the twenty-ninth week. The weight gain was normal, i.e., 8 kilograms, or 12 per cent.

The patient was admitted in premature labor in the thirty-fifth week. After an uneventful seven and one-fifth hour labor, a 2,070 Gm. living female

\*Normal values (100 per cent) taken to be as follows: N. P. N. = 50 mg. %;  $\text{CO}_2$  capacity = 65 vol. %; B. U. N. = 12.5 mg. %; Urea clearance, maximal = 55, standard = 54, 24 hour = 63 ml./min.; Blood uric acid = 2.0 mg. %; Uric acid clearance, short period = 14, 24 hour = 12.5. All clearances except the last ones are 24 hour clearances.

acid of 5.9, nonprotein nitrogen of 37.1, blood urea nitrogen of 16.9, and a  $\text{CO}_2$  combining power of 51.4 volumes per cent. At 7:15 p.m. of the same day the patient had an attack of generalized convulsions associated with unconsciousness, frothing at the mouth, and sphincter incontinence. Blood pressure was 205/110. Twenty minutes later, when venipuncture was being performed, a second convulsive attack occurred. Blood taken at this time showed no essential change. Neurological examination two hours later was negative, and likewise fundiscopic examination was again normal. There had been no past history of convulsions or of epilepsy. Hence, a repeat course of modified Stroganoff therapy was started. The blood pressure responded and returned to a normal range after nine days. The blood uric acid and nonprotein nitrogen gradually returned to normal.

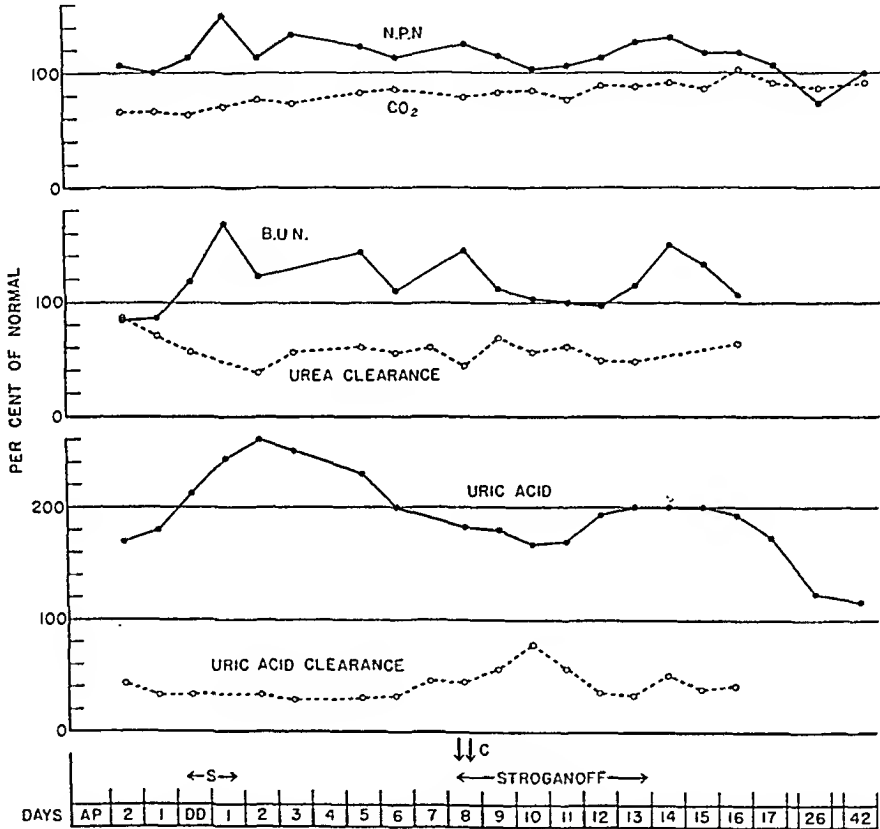


Fig. 5.—Case 3, laboratory findings.\*

The postpartum course was further complicated by a right lower lobe bronchopneumonia developing on the seventeenth day. The organism was alpha prime streptococcus. This secondary infection was attributed to aspiration at the time of the convulsions. Chemotherapy and penicillin were given. Notwithstanding, lung abscess occurred. This, in turn, improved with postural drainage and conservative therapy. The patient was finally discharged in good condition on the sixty-second postpartum day. The laboratory and other findings in this case are shown in Figs. 4 and 5. Diagnosis: Postpartum eclampsia.

### Discussion

*Clinical Findings.*—From a study of the clinical data relating to past history, blood pressure levels, water retention (edema), convulsive seizures, eye-

\*See footnote, p. 767.

pressures were elevated in the thirty-second week and in the thirty-fourth week; because of a blood pressure of 145/100 associated with two plus proteinuria and two plus edema, she was admitted for hospital care. The weight gain was not excessive, i.e., 9 kilograms, or 12 per cent, and the patient had no untoward symptoms.

The admission physical examination was normal, except for the presence of moderate edema and hypertension. The fetus was thought to be viable, although premature. Fundoscopic examination was normal. Blood uric acid was elevated to 5.5 mg., with a lowered  $\text{CO}_2$  combining power of 43.0 volumes per cent and a normal nonprotein nitrogen. Because the objective findings gradually became more pronounced, a modified Stroganoff management was started on the third day of hospitalization. Some temporary improvement resulted, although the urine output remained low, associated with an unabating proteinuria.

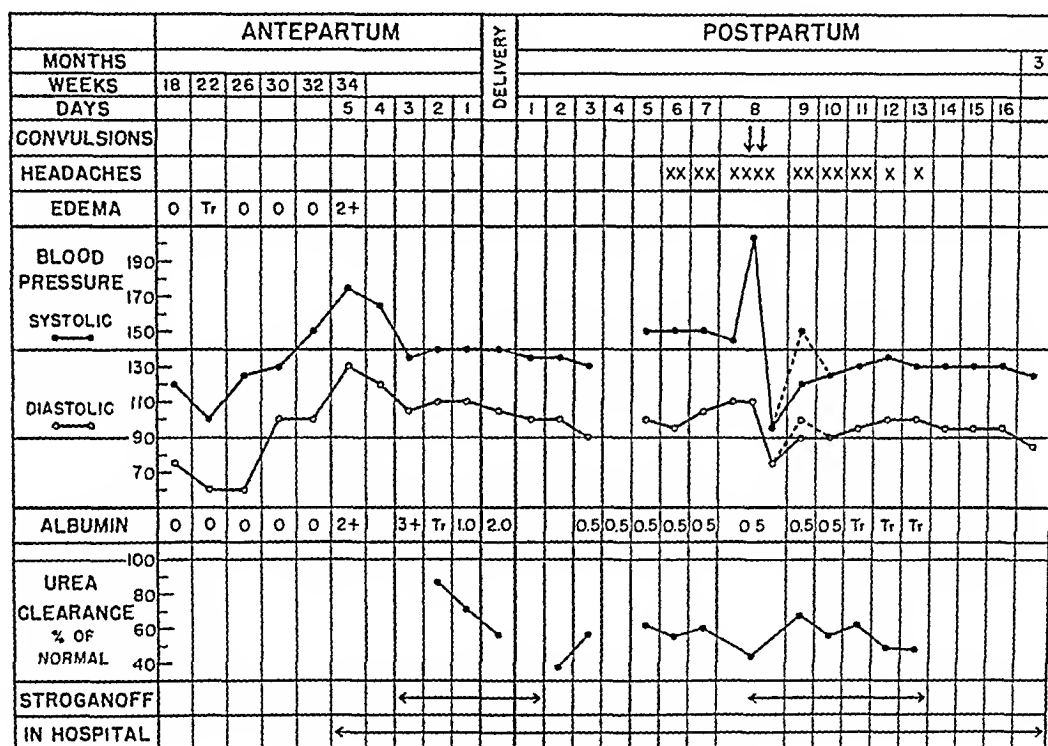


Fig. 4.—Case 3, clinical findings.\*

Labor set in spontaneously three days later; shortly thereafter the fetal heart was lost. After seven and two-thirds hours, a 2,130 Gm. deadborn male infant was spontaneously delivered. Measured blood loss was 500 c.c., and this was promptly replaced by transfusion. Immediately post partum the blood pressure was 150/110 and the blood uric acid was 6.4. A fever of  $38.0^{\circ}\text{C}$ . on the day of delivery and first postpartum day was attributed to dehydration. A Stroganoff treatment was discontinued the day following delivery because of improvement in the blood pressure and proteinuria. The blood uric acid, however, remained high. The postpartum course was uneventful through the seventh day, except for the development of persistent severe headache on the sixth day.

On the morning of the eighth day she again complained of severe occipital headache, and later in the day this was associated with blurring of vision. The blood pressure was 146/110 and the morning blood specimen showed a uric

\*See footnote, p. 766.

fied clinically as eclampsia and severe pre-eclampsia and, therefore, in conjunction with the clinical data, support the contention that these are actual instances of late postpartum eclampsia.

A review of the total 24 patients with postpartum eclampsia reveals that one had antepartum eclampsia, five suffered from severe pre-eclampsia eventuating in postpartum eclampsia, five had antepartum "toxemia" preceding the eclampsia, while thirteen women had no antepartum pre-eclampsia or "toxemia." In other words, in more than half of the cases, the postpartum eclampsia made its appearance without signs or symptoms indicative of toxemia during the antepartum or intrapartum periods. This is most significant in that eclampsia, although always associated with gestation, may occur days after delivery of the child and placenta in a woman apparently normal up to the time of the attack. From this it would almost seem as if the causative agent of the disease must be confined to the maternal organism, although undoubtedly activated or conditioned by the product of conception.

### Summary

Postpartum eclampsia may occur at any time during the first week of the puerperium. Three cases of late postpartum eclampsia are presented, one occurring on the fourth, one on the sixth, and one on the eighth day following delivery. Each of these showed most of the typical clinical and laboratory findings of eclampsia, namely, hypertension, albuminuria, edema, convulsions, elevated blood uric acid and decreased  $\text{CO}_2$  combining power, decreased uric acid clearance and decreased urinary output, followed by a complete return to normal after the eclampsia, with the single exception of persistent hypertension in one of the three patients.

### Reference

1. Bonsnes, R. W., and Stander, H. J.: *J. Clin. Investigation* 25: 378, 1946.

ground changes, urinary output, symptomatology, neurological signs, and subsequent follow-up findings in a toxemia clinic over extended periods, we feel amply justified in establishing the diagnosis of postpartum eclampsia in each of these three patients. It should be noted that in all three the outbreak of fits was preceded by signs and symptoms of "toxemia," and that in Case 1 hypertension persisted long after the disappearance of the eclampsia, while in Case 3, in which the first convulsion occurred on the eighth postpartum day, there was a return to normal, in all respects, nine days after the attack.

*Laboratory Findings.*—The chemical and other laboratory data, shown in the accompanying charts, are as convincing as the clinical findings, and substantiate the diagnosis of postpartum eclampsia.

In the first two cases the blood uric acid and the  $\text{CO}_2$  combining power behaved as in eclampsia, the former rising and the latter falling to moderately low levels. However, part of the increase in the blood uric acid in the first case may have been caused by the sodium lactate which was infused. The non-protein nitrogen and the urea levels remained essentially within normal limits in both these cases, although the first case shows a transient increase of questionable significance in the urea nitrogen, and therefore in the nonprotein nitrogen on the third and fourth days following the convulsions. A similar change in these values might possibly have occurred after the same relative time following the convulsions in the second case, but no data are available.

The blood findings in the third case are atypical, probably because this patient suffered from severe pre-eclampsia ante partum. It will be noted that there is a distinct elevation in the nonprotein nitrogen, uric acid, and urea nitrogen levels following delivery. These values then decrease slightly up to the time of the convulsive episode and are not altered markedly by it. Nor is there any particular change in the  $\text{CO}_2$  combining power at this time. However, a rise in the nonprotein nitrogen due to an increase in the urea nitrogen appears again as in the first two cases some days following the convulsive seizure; this time on the fifth and sixth days following the episode.

Kidney function with respect to urea and uric acid was followed in these cases by the procedures described by Bonsnes and Stander.<sup>1</sup> In the first case the urea clearance shows a depression which is reflected in the rise in the blood urea nitrogen. The uric acid clearance is generally low except for one day, but it seems to be improved by the twelfth day following the convulsion. In the second case the urea clearance was depressed and the uric acid clearance was normal on the two occasions when such tests were carried out (the second and eleventh days following the convulsions). No other data are available. In the third case the uric acid clearances were definitely depressed throughout the period in which they were studied.

It is not possible to interpret these laboratory findings at the present time. We have pointed out in the publication cited above that these changes in the blood levels of uric acid and urea can probably be attributed in large part to an alteration in kidney function. But such an interpretation does not seem to account for the changes observed in all cases. Yet, these laboratory findings are similar to those observed previously in cases which have been classi-



advantage of these forceps in their special field became more obvious in the successive years with the series of publications<sup>5, 6, 24</sup> on the mechanism of labor resulting from the x-ray studies of the pelvis.

Of most importance, so far as the Barton forceps were concerned, was the observation that the commonest position of the head during engagement was with the sagittal suture in a transverse diameter, and that a deep transverse position was a continuation of the position of engagement and not an incompletely rotated posterior.<sup>5, 6</sup> In small android and in flat pelvis it was particularly emphasized that the transverse position had to be maintained until much greater descent had been accomplished than usual because at or above the ischial spines rotation might be opposed by the lateral aspects of the prominent sacral alae.

In the less common anthropoid or transversely contracted pelvis the x-ray taught that the head often entered the pelvis as a direct anterior or posterior occiput, and that this position, once assumed, must necessarily be maintained throughout the passage of the bony pelvis. In such cases, and in others in which there is simply a narrow interspinous diameter, rotation from a posterior to an anterior, either spontaneously or by forceps, would require the forcing of a head already fixed in the anteroposterior through a narrower transverse diameter. For these cases in which rotation in the midplane of the pelvis is difficult for definite anatomic reasons, the Kielland forceps appeared to have a definite place, either to effect delivery of the head as a persistent occiput posterior, or else by elevation of the head above the brim or by traction to a lower place to permit rotation at a more favorable level.

Finally, since many of the problems in the midpelvis still concern an anterior occiput, or else an occiput that can be manually rotated in an ample pelvis to an anterior position, a classical forceps with typical cephalic and pelvic curves was required. The forceps commonly, but not exclusively, used for this was the Haig-Ferguson, a modification of the Simpson with light fenestrated blades, short handles, and a readily applied traction bar. The wide separation of the shanks in this instrument has appeared especially valuable in ensuring adequate protection of the baby's head.

The physical characteristics of these forceps and the technique of their application has been sufficiently described to require no repetition here. For the Barton forceps, reference may be made to the article of Barton, Caldwell, and Studdiford;<sup>3</sup> for the Kielland forceps, to the paper of Jarcho.<sup>15</sup> The original description of the Haig-Ferguson forceps is to be found in the Transactions of the Edinburgh Obstetrical Society.

The literature on the Kielland forceps is already immense and has been repeatedly reviewed (Greenhill;<sup>12</sup> Fink<sup>11</sup>). That the interest in this instrument continues in America is shown by several recent favorable reports (Rucker, Cosgrove,<sup>8</sup> Vedder<sup>25</sup>). Contributions on the use of the Barton forceps are, however, extremely meager, being practically limited to the article just cited and to a series of 55 cases published by Bachman in 1927.

## THE SELECTION OF FORCEPS FOR MIDPELVIC ARREST OF THE VERTEX

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**S**TUDIES of the results of forceps delivery have more or less evaded statistical analysis. It has not been possible to compare the effectiveness of one instrument or one maneuver with another, for such factors as the relative skill of the operator and, even more, the range of the indications for the operation, are of enormous importance in determining the outcome. Nevertheless, mid-pelvic arrest of the vertex remains, perhaps, the most difficult and inaccessible problem in clinical obstetrics. An attempt to reduce this problem to terms by which statistical study and comparisons may be made is therefore indicated.

The principle to be followed in the selection of forceps for delivery of the vertex arrested or delayed in the midpelvis has produced at least two schools of thought. One has maintained that the practitioner or obstetrician should so thoroughly familiarize himself with one type of forceps that he can apply it, possibly after manual adjustment of the head, to any situation which may arise with the vertex presenting. The second school believes that no forceps is mechanically adapted to all vertex deliveries and that special types must be selected for application to particular positions of the occiput or to effect delivery through the most favorable diameters of the pelvis.

The selection of one of several instruments to meet each particular problem has been the practice on the Bellevue Hospital Obstetrical Service during recent years. Indications have not been standardized, and considerable freedom has been left to individual operators, both attending and resident physicians, to make their own choice of forceps. Nevertheless, a more or less consistent system has developed which is now generally followed.

The factors responsible for the development of this attitude toward the midforceps problem are to be found partly in the availability to members of the division of several types of forceps of radically different design and partly from the growing appreciation of pelvic architecture as a determining factor in the mechanism of labor.

### The Theoretical Need of Several Types of Forceps

When, in 1934, the first cases of this report were being delivered, the Kielland forceps had already been used for many years on the service, and its value, particularly in posterior positions, was partly realized. At about this time the Barton forceps was introduced to the hospital and immediately found an important place in the control of deep transverse arrest. The theoretical

TABLE I. EVOLUTION OF ATTITUDE TOWARD SELECTION OF FORCEPS

YEAR	TOTAL	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
Classical forceps	196	46%	41%	36%	20%	18%	24%	28%	32%	24%	6%	18%	20%
Barton forceps	371	37%	26%	36%	65%	70%	69%	60%	61%	72%	81%	56%	47%
Kielland forceps	134	17%	33%	28%	15%	12%	7%	11%	7%	4%	12%	26%	32%
Total mid-forceps	701	52	102	107	82	43	45	53	41	46	48	50	34

TABLE II. POSITION OF FETAL HEAD IN RELATION TO TYPE OF FORCEPS SELECTED. PERCENTAGE OF INSTANCES OF A GIVEN POSITION OF THE OCCIPUT DELIVERED WITH EACH TYPE OF FORCEPS

	TOTAL	ANTERIOR		TRANSVERSE		POSTERIOR			FACE	BROW
		LOA	ROA	LOT	ROT	LOP	ROP	OP		
Classical forceps	196	98%	95%	11%	6%	27%	7%	38%	25%	-
Barton forceps	371	-	-	75%	87%	29%	33%	-	25%	100%
Kielland forceps	134	2%	5%	14%	7%	44%	60%	62%	50%	-
Total mid-forceps	701	101	44	191	206	34	112	8	4	1

TABLE III. TYPES OF PELVIS IN X-RAYED CASES IN RELATION TO FORCEPS SELECTED

	TOTAL	GYNECOID				ANDROID				PLATY-PELLOID	ANTHRO-POID	
	TOTAL CASES X-RAYED	PURE TYPE	AN-DROID TEND-ENCY	PLATY-PEL-LOID TEND-ENCY	AN-THRO-POID TEND-ENCY	PURE TYPE	GYNE-COID TEND-ENCY	PLATY-PELLOID TEND-ENCY	AN-THRO-POID TEND-ENCY	PURE PLATY-PELLOID TYPE	PURE TYPE	GYNE-COID TEND-ENCY
Classical forceps	50	33	2	1	5	2	3	1	0	0	2	1
Barton forceps	130	66	6	18	9	3	12	3	1	8	1	3
Kielland forceps	63	26	5	5	12	3	2	1	1	0	7	1

TABLE IV. THE LENGTH OF THE TRUE CONJUGATE IN RELATION TO FORCEPS SELECTED

ANTEROPOSTERIOR DIAMETER OF INLET IN CENTIMETERS	8 TO 8.9	9 TO 9.9	10 TO 10.9	11 AND OVER	TOTAL
Classical forceps	1	7	23	93	124
Barton forceps	10	28	48	158	244
Kielland forceps	2	8	26	56	92
Total estimated cases	13	43	97	307	460

For the anteroposterior diameter of the inlet x-ray measurements were utilized in cases so studied, and clinical estimation only in the remainder.

TABLE V. WEIGHT OF BABY IN RELATION TO FORCEPS SELECTED

	TOTAL CASES	PER CENT UNDER 7 POUNDS	PER CENT 7 TO 8 POUNDS	PER CENT 8 TO 9 POUNDS	PER CENT OVER 9 POUNDS
Classical forceps	196	34	35	23	8
Barton forceps	371	31	35	26	8
Kielland forceps	134	29	34	26	10
Total	701	31	35	26	8

## The Material Analyzed

The material for this analysis consisted in the 701 midforceps operations occurring among 10,814 deliveries on the Obstetrical Service of Bellevue Hospital from January 1, 1934, to December 31, 1945. In considering the results obtained and some of the inconsistencies in application, it is necessary to remember that the time of the report covers the service of twelve residents who were supervised at one time or another by 20 different attendings. It may be noted also that the Bellevue Service must accept new patients and transfers from other hospitals at any time, and that only three-fourths of the cases delivered were registered in the antepartum clinic of the service or subject to study before the onset of labor.

### Factors Influencing the Selection of Forceps in Individual Cases

In reviewing the midforceps of the years 1934 to 1940, it is clear that various factors influenced the selection of forceps for each case.

1. *Experience*.—With the introduction of any new instrument there will be a period of trial during which staff members are learning its use. Thereafter, it may increase in popularity or else be gradually dropped. It is to the credit of the Barton forceps that its popularity steadily increased until about over half of all midforceps cases were treated with this instrument (Table I).

2. *Position of the Occiput*.—Undoubtedly the most important point on which the selection of forceps is made on the Bellevue Service is the position of the occiput. Table II shows that among the cases with anterior positions, classical forceps have been used almost without exception. In the transverse positions, about three-fourths were delivered with the Barton, while in the posteriors, over 50 per cent were delivered with the Kiellands.

The figures in Table II become clear only when it is noted that in many instances an attempt was made manually to rotate the posterior occiput to a transverse or oblique position in order to permit the use of the Barton instead of the Kielland forceps. Attempts were sometimes made also to convert the transverse to an anterior position so that the classical forceps might be used, but the growing confidence in the Barton forceps when the sagittal suture was found in the transverse led to an acceptance of this as a favorable position for application.

The relative frequency with which the several positions of the occiput are recorded is undoubtedly somewhat influenced by the obstetrician's preference as to technique of delivery. Transverse positions have been reported previously as occurring in one-fifth to one-third of all cases.<sup>7, 19, 20</sup> It is interesting that on the Bellevue Service, where on account of the Barton forceps the transverse position was not considered particularly unfavorable, its incidence rose to 51 per cent, a figure approaching that found in x-ray studies.<sup>5-6</sup>

3. *Type of Pelvis*.—Since the Kielland and Barton forceps were used predominantly for cases in which the position was transverse or posterior, and since it has been shown that there is a tendency for these positions to persist in android and anthropoid pelvises<sup>5, 6, 24</sup> it might be expected that these less favorable types would be commoner among the groups of cases delivered by the Barton or Kielland forceps. From a review of the 243 cases on which diagnosis was made by stereoscopic roentgenogram of the pelvis, there was some evidence of this tendency (Table III). Further, if the prognosis to mother or baby is adversely affected by these pelvises, one must recognize at once that the Barton and Kielland forceps were given more difficult tasks than the classical forceps. Table IV shows also that contraction of the inlet was more common in the cases in which these special forceps were applied than in those in which the classical forceps were used.

ceps. Blood loss of over 500 c.c. was somewhat commoner after the use of the Kielland forceps, but there was no accompanying record of increase in vaginal lacerations. The deep and early episiotomies usually needed with the Kielland forceps offer a partial explanation. The three bladder injuries following Barton forceps are noteworthy, but all were very small, and in each instance the fistula closed spontaneously.

4. *Fetal Mortality*.—When one comes to the results for the fetus there appears a decided difference in the performance of the three instruments. The gross fetal mortality, stillborn and neonatal, for the entire group of 701 cases, was 9.4 per cent. If the fetal deaths due to causes other than intracranial injury are subtracted, the mortality apparently directly ascribable to the operation becomes 5.2 per cent.

The uncorrected mortality for the three instruments was found to be the following: for the classical forceps, 8.6 per cent; for the Barton, 7.5 per cent; and for the Kielland, 15.6 per cent. When only fetal deaths due to the operation are considered, the contrast becomes still more striking, for then the mortality for the classical forceps and the Barton is only 3.5 per cent and 3.7 per cent, respectively, while that for the Kielland was about three times as high, namely, 11.9 per cent (Table VII).

This difference deserves immediate comment. In partial extenuation of the record for the Kielland, it may be noted that a greater proportion of posteriors were delivered by this instrument than by any other and, further, that in 5 of 16 deaths ascribed to the Kielland forceps other instruments had been applied without success. On the other hand, many posteriors, as well as the great majority of transversely arrested heads, were delivered by the Barton forceps with strikingly good infant results. The low incidence of intracranial injury with these forceps is probably to be ascribed in part to the possibility of perfect cephalic application to the transversely placed head, and further to the fact that rotation is accomplished deep in the pelvis where bony opposition is at a minimum.

5. *Failure of Forceps*.—In the classification of the 701 patients, each case was assigned to the forceps which had accomplished the principal part of the delivery. Actually, in 99 of these patients more than one type of forceps was employed (Table VIII). Usually the second forceps was applied to complete

TABLE VIII. USE OF MORE THAN ONE INSTRUMENT TO EFFECT DELIVERY

TYPE OF FORCEPS FIRST APPLIED	TYPE OF FORCEPS WITH WHICH DELIVERY WAS COMPLETED		
	CLASSICAL TOTAL CASES	BARTON TOTAL CASES	KIELLAND TOTAL CASES
Classical	211	183	24
Barton	357	30	13
Kielland	132	18	9
			104

delivery after the first instrument had accomplished its purpose of rotation, but in about a third the second instrument was used after admitted failure of the first.

Classical forceps were first applied in 211 cases and were used to complete delivery in 183 of these. The 29 cases remaining were handled in 24 instances by the Barton, in four by the Kielland, and in one by version and extraction. These cases represent, in almost all instances, failures with the classical forceps.

The Barton forceps were the first instrument applied in 314 cases. In 21 cases, after successful rotation on the pelvic floor, the Barton forceps were replaced and delivery completed by a classical forceps as a method of choice.

4. *Size of Baby.*—Large babies were distributed about equally throughout the different groups. The Kielland forceps proved more unsuitable, the babies over 8 pounds in weight being slightly more common in the group in which it was used (Table V).

TABLE VI. MATERNAL RESULTS WITH VARIOUS TYPES OF FORCEPS

	TOTAL CASES	MATERNAL DEATHS	PERCENTAGE OF MORBIDITY	PERCENTAGE OF CASES WITH BLOOD LOSS OVER 500 C.C.	INJURIES TO THE BIRTH CANAL, ACTUAL NUMBER OF CASES				
					CERVICAL LACERATIONS	SULCUS TEARS OF VAGINA	VESICOVAGINAL FISTULAS	THIRD DEGREE LACERATIONS OF PERINEUM	
Classical forceps	196	2	34.1	13.2	7	12	0	1	
Barton forceps	371	2	42	13.2	38	47	3	2	
Kielland forceps	134	0	49.9	18.6	10	20	0	0	
Total	701	4	41.3	14.2	55	79	3	3	

TABLE VII. FETAL RESULTS WITH VARIOUS TYPES OF FORCEPS

	FETAL AND NEONATAL DEATHS TOTAL			FETAL AND NEONATAL DEATHS INTRACRANIAL INJURY	
	TOTAL	NUMBER	PER CENT	NUMBER	PER CENT
Classical	196	17	8.6	7	3.5
Barton	371	28	7.5	14	3.7
Kielland	134	21	15.6	16	11.9
Total	701	66	9.4	37	5.2

### Results With Different Types of Forceps

The results of the use of these forceps may be considered under the headings of maternal mortality and morbidity, injuries to the birth canal, hemorrhage, and fetal mortality (Tables VI and VII).

1. *Maternal Mortality.*—There were four maternal deaths (0.56) in the series of 701 patients, two of these having been delivered by classical forceps and two by the Barton. One of these deaths, following delivery by the classical forceps, occurred in a patient receiving an intravenous infusion of toxic gum acacia that was responsible for other deaths in the hospital at about the same time. The remaining three patients died of puerperal sepsis and, although there was no gross injury, these deaths must be ascribed to the type of delivery. The corrected maternal mortality rate for midforceps deliveries was therefore only 0.4 per cent.

2. *Maternal Morbidity.*—On the basis of the standard of morbidity followed by the Bellevue Obstetrical Service, namely, a rise to 100.4° F. on at least one occasion on two separate days post partum, 41.3 per cent of the entire series of forceps cases were morbid (Table VI). The cases delivered by classical forceps had a somewhat better record than those in the Barton and Kielland groups.

3. *Injuries to Birth Canal.*—On the basis of the statistics of Table VI, it is difficult to find points for drawing comparison between the three types of for-

30 infant deaths among 222 deliveries by hysterotomy, or 13.5 per cent. Analysis of these deaths showed, however, that 12 were from abdominal deliveries carried out for the termination of pregnancy before the period of viability, that 10 were in cases of premature separation, two in rupture of the uterus, and one in placenta previa, and that one followed a postmortem section, and one was in a baby with congenital anomalies incompatible with life. There were only three deaths possibly attributable to the method of delivery, one being the baby of a tuberculous mother, and two being born after over fifteen hours of labor. There were no deaths of term babies in uncomplicated pregnancies delivered by elective section.

The complicated character of the problem of dystocia leading to midpelvic arrest is manifest in the variety of plans adopted by different obstetric services in attempting to solve it. The most important variables that are being tested in this way are (1) the frequency of cesarean section; (2) the conduct of the second stage, in particular with respect to its length; and (3) the technique of forceps application. Difference in attitude toward the first two of these will greatly affect forceps incidence and forceps difficulty and make it almost impossible to compare the relative value of different types of instruments and techniques of application on any statistical basis.

1. *The Cesarean Section Rate.*—A high incidence of cesarean section will be accompanied by a decreased frequency of forceps delivery and improved figures for that procedure, since it will in general be the difficult cases of borderline pelvis, large babies, malposition and "cervical dystocia" that are transferred to the cesarean section column. A low incidence of cesarean section might be expected to increase the burden placed on the forceps and would probably raise both the total and the percentage of bad results from this instrument.

2. *Attitude Toward Proper Length of Second Stage.*—If only a short second stage is permitted before operative delivery is resorted to, forceps will frequently be applied, but the percentage of bad results should be low, since many relatively easy cases will fall in the forceps column. On the other hand, if the policy is followed of supporting a patient, a long second stage and of giving small doses of pituitrin in selected cases, the use of forceps in the midpelvis may be reduced almost to the vanishing point (Eastman). The few forceps deliveries which remain to be done, however, will be only the more difficult and the percentage, although not the total, of poor results may be high.

3. *Technique of Forceps Application and Delivery.*—The selection of one or another of the many types of instruments, the employment of manual correction of position, the level at which rotation is carried out, and a list of other technical points may also have some bearing on the results.

Search of the literature for guidance on these three particular factors yields no authoritative information. Maternal deaths from the forceps operation alone are actually so infrequent that comparisons on this basis are not very useful. In reports published since 1930, figures showing stillbirth and neonatal death rates following forceps deliveries have ranged from practically nothing to 20 per cent. Infant deaths following midforceps, based on all operation and not selected groups, have been reported with the following frequency: 2.3 per cent, Kane and Parker<sup>16</sup>; 5.0 per cent, Potter and Adair<sup>21</sup>; 5.4 per cent, Acken<sup>1</sup>; 6.4 per cent, Erblich<sup>2</sup>; and 6.8 per cent, Hoffstrom.<sup>13</sup> Series of cases in which no distinction was made between applications at different

but not of necessity. In the others Barton forceps were admitted failures, delivery being accomplished by one of the other instruments.

The Kielland forceps were used to complete 104 of the deliveries in which it was the original instrument applied. After successful rotation of the head to an anterior or transverse position the Kielland was removed and, in 17 instances, delivery was accomplished by classical, and in eight by the Barton forceps. In two instances the Kielland failed not only to effect delivery but also failed in rotation.

### The Present Bellevue Technique

The present plan of handling midpelvic arrest on the Bellevue service, as developed from the experience just analyzed, may be outlined as follows:

With the occiput in an anterior position, the classical forceps, usually of the Haig-Ferguson type, are employed. If the occiput has successfully reached this position it can usually be assumed that descent in the transverse is no longer necessary.

With the occiput in the transverse, it is felt that this diameter is usually the best for further descent, although with a gynecoid pelvis attempts to rotate manually to an oblique position may be undertaken. If rotation is easily accomplished manually, the classical forceps are employed; otherwise descent is accomplished with the Barton forceps. In cases with an android or flat pelvis, on the other hand, and especially with forward displacement of the sacrum, manual rotation may be impossible, and continued descent in the transverse with the aid of the Barton forceps is particularly desirable. If the Barton forceps are used, rotation is carried out when crowning first occurs, and delivery can be completed with this instrument, if desired.

In posterior position, rotation, either manual or with the forceps, may be attempted in the anthropoid or transversely contracted type of pelvis, but sometimes fails. Under these circumstances the Kielland has been the instrument of choice. Whereas, in the early part of the period reported, upward displacement of the head with its rotation above the pelvic brim was frequently resorted to; this technique has recently been used with decreasing frequency. The present procedure of choice is an attempt at rotation in the midpelvis if the type of pelvis is favorable. Otherwise traction is made with the occiput still posterior, and delivery carried out with the vertex in that position or after rotation on the pelvic floor.

### Discussion of Results

The importance of the midforceps problem can be best seen from a glance at the contribution of this procedure to the maternal and fetal mortality on the Bellevue Obstetrical Service. From June 1, 1934, to May 31, 1941, there were 40 maternal deaths, a rate of 3.7 per thousand deliveries. The fact that only four of these occurred in patients delivered by midforceps indicates that this procedure did not add greatly to the total maternal mortality.

During the years noted, there was a total of 227 deaths of term infants or stillbirths and neonatal death rate in this group of 2.48 per cent. Among the midforceps cases there were 41 deaths, stillborn and neonatal, among the 465 infants weighing over 5 pounds. This rate of 8.8 per cent indicates that midforceps delivery does materially increase the risk run by the term infant.

For contrast, it is interesting to consider the mortality among babies delivered by cesarean section. During the period under consideration there were



2. In this series the Barton forceps was used in 371 instances, the Kielland in 134, and some form of classical instrument in 196. The gross infant mortality for the entire series was 9.4 per cent, the death rate for the Kielland delivered babies being higher than for those handled by the other types.

3. The results of forceps deliveries cannot be examined as isolated figures, but only in relation to the conditions under which they were performed. Reports published in the literature show an infant mortality from forceps ranging from 2.3 to 20.0 per cent, but such reports have usually failed to state underlying conditions and cannot, therefore, be used to demonstrate the relative merits of different techniques.

4. The problem of handling cases of actual or potential arrest in the mid-pelvis is evidently to be solved as much by studying the effects of varying the incidence of cesarean section or the management of the second stage as by improving the special technique employed in the forceps operation.

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levels have sometimes shown higher figures, such as 10.0 per cent (Stander<sup>23</sup>); 13.6 per cent (Puppel<sup>22</sup>) and 20.08 per cent (Novey<sup>18</sup>). Since, however, the exact conditions under which these operations were carried out are rarely stated by the authors of the reports, it is not possible to tell what special factors are placed in contrast by the observed differences in results.

The basic conditions under which the midforceps operation has been performed at Bellevue since 1934 are as follows: (1) The cesarean section rate is fairly low, varying from 1.8 to 4.3 per cent (Table IX). (2) In the absence

TABLE IX. FREQUENCY OF MIDFORCEPS IN RELATION TO OTHER OBSTETRIC OPERATIONS

	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
Total delivered patients	1691	1710	1510	1462	1459	1535	1447	1496	1625	1411	1353	1461
Percentage of operative deliveries	11.6	15.3	19.2	16.0	14.6	13.1	13.8	13.6	12.5	15.7	13.9	14.1
Percentage of cesarean sections	2.6	2.5	2.8	2.8	2.2	1.8	1.9	2.2	2.38	2.7	2.4	4.3
Percentage of high forceps	0.53	0.17	0.06	0.34	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Percentage of low forceps	3.7	5.0	7.3	5.9	17.0	6.9	7.3	8.0	7.1	8.3	6.7	6.8
Percentage of midforceps	3.1	5.6	7.0	5.6	2.9	2.8	3.8	2.7	2.2	3.4	3.7	2.1

TABLE X. FETAL DEATHS IN CASES DELIVERED BY MIDFORCEPS BY YEARS

	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
<i>Classical:</i>												
Total cases	30	45	43	20	11	11	16	13	11	3	9	7
Deaths	5	6	3	0	0	1	4	2	1	1	0	0
<i>Barton:</i>												
Total cases	13	25	39	50	30	28	31	25	33	39	28	15
Deaths	2	0	2	7	2	3	1	4	2	3	3	1
<i>Kielland:</i>												
Total cases	9	32	25	12	5	3	6	3	2	6	13	11
Deaths	5	6	0	3	1	1	0	0	0	0	1	1
Total												
All cases	52	102	117	72	46	42	53	41	46	48	50	34
Deaths	12	12	5	10	3	5	5	6	3	4	4	2

of progress a second stage of one hour in multigravida and two hours in primigravida before intervention is the rule in otherwise normal cases, but this period may be prolonged if mother and infant are in good condition. (3) The forceps technique has been based, as outlined, on the selection of one of several instruments believed to be especially adapted to the individual pelvis and the particular position of the vertex encountered. Under these conditions the midforceps operation on the Service resulted in a total stillbirth and neonatal death rate of 9.4 per cent. The deaths due to intracranial injury, that is to say, those directly attributable to the forceps operation, amounted to 5.2 per cent.

### Summary and Conclusions

1. Report is made of 701 midforceps deliveries carried out on the basis of the general principle that a given type of pelvis and a given position of the vertex may indicate the selection of a special type of instrument.

TABLE 1. B VITAMINS

SUB- JECT	WEIGHT		TOTAL THIAMINE			FREE THIAMINE			TOTAL RIBOFLAVIN			FREE RIB	
			TOTAL	PER 100	PER	TOTAL	PER 100	PER	TOTAL	PER 100	PER	TOTAL	PER 100
	FRESH	DRY		GRAMS FRESH	GRAM DRY		GRAMS FRESH	GRAM DRY		GRAMS FRESH	GRAM DRY		GRAMS FRESH
	GM.	GM.	μG.	WEIGHT μG.	WEIGHT μG.	μG.	WEIGHT μG.	WEIGHT μG.	μG.	WEIGHT μG.	WEIGHT μG.	μG.	WEIGHT μG.
L. F.	661	96	381	58	4.0	131	20	1.4	1,480	224	15.4	311	47
V. G.	453	70	187	41	2.7	72	16	1.0	792	175	11.4	212	47
V. K.	327	45	193	59	4.3	44	13	1.0	583	178	12.9	168	51
V. L.	414	58	222	54	3.8	64	15	1.1	697	168	12.0	265	64
J. M.	592	90	382	64	4.2	105	18	1.2	958	162	10.6	261	44
D. M.	998	64	252	25	3.9	104	10	1.6	613	61	9.5	303	30
C. O.	713	58	197	28	3.4	47	6	0.8	626	88	10.7	211	30
V. S.	444	68	264	59	3.9	80	18	1.2	759	171	11.1	371	84
A. S.	642	96	231	36	2.4	112	17	1.2	869	135	9.0	566	88
Average	583	72	256	47	3.6	84	15	1.2	820	151	11.4	296	54

The average value for free thiamine in the placenta was 15  $\mu$ g. per 100 Gm. of wet tissue, varying from 6 to 20  $\mu$ g. (Table I). The bound thiamine varied from 15 to 46  $\mu$ g. averaging 32  $\mu$ g. per 100 Gm., or 68 per cent of the total. The ratio of free to bound thiamine was 1 to 2.1.

After determining the free and bound thiamine in retroplacental blood Neuweiler<sup>8</sup> obtained a ratio of 1 to 3.5. He also found that free thiamine in the mother's blood decreased from 5.1 at the beginning of labor to 3.2  $\mu$ g. per 100 Gm. at delivery, but found no change in bound thiamine, which averaged 11.3 and 11.6  $\mu$ g. per 100 Gm. at the beginning and end of labor, respectively. The retroplacental blood contained approximately the amounts of thiamine in the mother's blood after the birth of the child, 3.4  $\mu$ g. of free and 11.8  $\mu$ g. of bound thiamine per 100 Gm. He ascribes this decrease in the mother's blood thiamine and the low value for the retroplacental blood to several reasons: first, and chiefly, to the increased synthesis of acetyl choline, with which the placenta is richly supplied and which is one of the factors initiating muscular contractions in the birth process; second, to the changes in the energy system; and finally, to an increased transmission of free thiamine through the placenta during the process of birth, for as a result of the muscular contractions the amount of blood collecting in the uterus is very large and the fetus is better supplied with oxygen. It is logical that other substances, such as thiamine, pass the placental barrier in increased amounts. Since, according to Neuweiler, only free thiamine is transmitted to the fetus and the bound is not, it is understandable that only free thiamine decreases in the mother's blood and the level of the bound fraction remains unchanged. The lower concentration in the retroplacental blood is in striking contrast to the higher concentration of ascorbic acid found by Neuweiler. He states that this difference between thiamine and ascorbic acid reflects the fact that the placenta stores ascorbic acid, but under normal conditions does not store thiamine to the same extent. The higher ascorbic acid concentration in the retroplacental blood depends, therefore, in his belief, on the output of ascorbic acid stored in the placenta.

In his earlier article Neuweiler<sup>5</sup> noted that the venous cord blood had a higher content of thiamine than the arterial blood, which he concluded was the result of absorption from the placenta. Also, after injecting thiamine into the mother before the child's birth, he noted an increase of thiamine in the placenta. From these results he thought that the placenta might possess some ability to store thiamine, to guarantee the fetus a supply independent of fluctuations in the maternal diet, and affording protection from an excess of thiamine which might exert an unfavorable influence on sugar metabolism. In his later work<sup>5</sup> he states that the placenta evidently does not store thiamine as

# COMPOSITION OF THE HUMAN PLACENTA

## III. Vitamin Content

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IN THE last decade much information has been published concerning the vitamin content of the human placenta, with special emphasis on the ability of the organ to store nutriment and to bar their passage to the fetus. From these reports it seems that the placenta stores ascorbic acid quite readily, likewise vitamin D, while thiamine is absorbed to a lesser extent, and vitamin A and carotene only in very small quantities. The placenta seems to serve as a regulatory device for some of the vitamins, letting only required amounts pass to the fetus. Data on the niacin, pantothenic acid, and biotin contents of human placenta have not been published in the available literature. In the present study thiamine, riboflavin, pantothenic acid, niacin, and biotin have been determined in nine human placentas.\* The collection and preparation of the material have been described in a preceding paper.<sup>1</sup>

Although the general microbiological procedures used in the analysis of human milk have been described,<sup>2-4</sup> the dried placenta required somewhat different preparation for pantothenic acid and biotin assays. (For niacin, the placenta samples were autoclaved with 0.1 N HCl as were the milk samples, since alkali or stronger acids did not increase the values obtained. There is, therefore, no "precursor" of niacin in placental tissue.) In determining pantothenic acid, the placentas were incubated with mylase P at pH 4.6 for forty hours at 37° C. With water extraction alone the values were 15 to 30 per cent lower. The "loosely bound" and the "firmly bound" biotin values were obtained after autoclaving with 0.1 N HCl for one-half hour, and 2 N HCl for three hours, respectively. Stronger acids or longer periods of autoclaving did not increase the biotin values.

### Thiamine

The total amount of thiamine per placenta averaged 256 micrograms, of which 84  $\mu$ g. was free thiamine and 172  $\mu$ g. was bound thiamine (Table I).

The average amount of total thiamine per 100 Gm. of placental tissue was 47  $\mu$ g. within a range of 25 to 64  $\mu$ g. per 100 Gm. Neuweiler,<sup>5</sup> using Ritsert's thiochrome method, found lower values than this, his average for 14 mature placentas being 5.9  $\mu$ g. per 100 Gm., with a range of 2.7 to 10  $\mu$ g. Gachtgen's<sup>6</sup> values for placental thiamine are similar to those of Neuweiler, but Dubrausky and Lajos,<sup>7</sup> using Willstadt's colorimetric method, reported values ranging from 108 to 980  $\mu$ g. per 100 Gm. for 25 mature placentas averaging 370  $\mu$ g. These high values approach those obtained by Neuweiler after injecting the mother with thiamine, and he ascribed the high results of Dubrausky and Lajos to either a better nutritional state of their subjects or to the use of a different method of analysis, or possibly to a combination of both.

\*The investigation of the composition of the placenta was a part of studies of mothers during pregnancy and lactation, the composition of their milk, and the growth of their infants. Partial support for the investigation was given by the Nutrition Foundation, Inc.

lung, muscle, skin, mammary gland, and seminal ducts, but are lower than their values for heart, liver, kidney, spleen, adrenals, stomach, ileum, and ovary. On a dry weight basis, the placenta values exceed the amounts reported<sup>10</sup> for skin, mammary gland, and seminal ducts, but compare well with the values for colon, testes, brain, lung, and muscle.

### Niacin

In the nine placentas the amounts of niacin ranged from 7.64 to 17.43 mg., averaging 10.79 mg. per placenta (Table I). The placenta tissue averaged 151  $\mu$ g. per Gm. of dry material, a value almost as high as those published for liver and kidney,<sup>10</sup> 202 and 196  $\mu$ g. per Gm. dry weight, respectively, and similar to those for muscle and heart tissues.

The placenta contained 1.99 mg. of niacin per 100 Gm. of fresh tissue, an amount equal to or greater than the amounts found in other tissues by Taylor, Pollack, and Williams,<sup>10</sup> with the exception of heart, liver, kidney, and muscle.

### Pantothenic Acid

The average amount of pantothenic acid per placenta was 1,535  $\mu$ g., within a range of 854 to 3,043  $\mu$ g. (Table I). Per gram of dry material the average, 20.8  $\mu$ g., is higher than values which have been found<sup>10</sup> for skin, muscle, mammary gland, and seminal ducts, and approximates the amounts found in spleen, adrenal glands, ovary, stomach, ileum, and lung. The contents reported for heart, liver, kidney, brain, colon, and testes far exceed the amount in placenta tissue.

On a wet weight basis the pantothenic acid content of placenta, 279  $\mu$ g. per 100 Gm., is lower than the amounts in all the tissues analyzed by Taylor, Pollack, and Williams,<sup>10</sup> except skin, seminal ducts, ovary, and mammary gland.

### Biotin

The total amount of firmly bound biotin per placenta averaged 8.9  $\mu$ g., ranging from 5.4 to 16.5 (Table I). The loosely bound\* fraction was about one-fourth of the total biotin. The dry placenta tissue contained 0.12  $\mu$ g. of firmly bound biotin per gram, an amount higher than that reported by Taylor, Pollack, and Williams<sup>10</sup> for skin and approximating their values for lung, muscle, ovary, and seminal ducts. It is much lower than their values for tissues such as liver or kidney, which averaged 2.4 and 3.5 mmg. per Gm., respectively.

TABLE II. RELATIONSHIPS BETWEEN VITAMIN CONTENTS AND HEAT OF COMBUSTION OF HUMAN PLACENTA

SUBJECT	THIAMINE		RIBOFLAVIN	NIACIN	RATIO	
	PER 1000 CALORIES MG.	PER 1000 CALORIES NOT FAT MG.	PER 1000 CALORIES MG.	PER 1000 CALORIES MG.	THIAMINE TO RIBOFLAVIN	THIAMINE TO NIACIN
L.F.	0.75	0.81	2.90	34.2	0.26	0.022
V.G.	0.54	0.58	2.30	28.7	0.24	0.019
V.K.	0.81	0.88	2.46	32.2	0.33	0.025
V.L.	0.72	0.78	2.28	30.2	0.32	0.024
J.M.	0.86	0.94	2.16	29.4	0.40	0.029
D.M.	0.74	0.79	1.79	26.3	0.41	0.028
C.O.	0.64	0.68	2.02	25.5	0.32	0.025
V.S.	0.73	0.79	2.10	30.5	0.35	0.024
A.S.	0.51	0.54	1.93	26.4	0.27	0.019
Average	0.70	0.75	2.23	29.3	0.31	0.024

\*The loosely bound was determined by autoclaving 30 minutes with 0.1 normal hydrochloric acid, while the firmly bound was released by autoclaving 2 hours with 2 normal hydrochloric acid.

## IN HUMAN PLACENTA

OFLAVIN				PANTOTHENIC ACID			BIOTIN, FIRMLY BOUND			BIOTIN, LOOSELY BOUND		
PER GRAM DRY		PER 100 GRAMS FRESH	PER GRAM DRY		PER 100 GRAMS FRESH	PER GRAMS DRY		PER 100 GRAMS FRESH	PER GRAM DRY		PER 100 GRAMS FRESH	PER GRAM DRY
WEIGHT μG.	TOTAL MG.	WEIGHT MG.	WEIGHT MG.	TOTAL μG.	WEIGHT μG.	WEIGHT μG.	TOTAL μG.	WEIGHT μG.	WEIGHT μG.	TOTAL μG.	WEIGHT μG.	WEIGHT μG.
3.2	17.43	2.64	0.18	3043	460	31.6	16.5	2.5	0.17	4.2	0.6	0.04
3.0	9.90	2.18	0.14	1206	266	17.3	8.7	1.9	0.12	1.4	0.3	0.02
3.7	7.64	2.34	0.17	854	261	18.9	5.4	1.6	0.12	1.6	0.5	0.03
4.6	9.25	2.23	0.16	1443	348	24.8	7.6	1.8	0.13	1.6	0.4	0.03
2.9	13.05	2.20	0.14	1899	321	21.1	10.8	1.8	0.12	1.8	0.3	0.02
4.7	9.00	0.90	0.14	1061	106	16.5	6.9	0.7	0.11	1.2	0.1	0.02
3.6	7.88	1.10	0.14	964	135	16.5	6.1	0.8	0.10	1.5	0.2	0.03
5.4	11.03	2.48	0.16	1403	316	20.6	8.6	1.9	0.13	1.8	0.4	0.03
5.9	11.90	1.85	0.12	1939	302	20.2	9.8	1.5	0.10	2.8	0.4	0.03
4.1	10.79	1.99	0.15	1535	279	20.8	8.9	1.6	0.12	2.0	0.4	0.03

readily as it does ascorbic acid, but rather acts as an active barrier regulating the amounts of thiamine that pass through to the fetus.

The studies of Neuweiler<sup>9</sup> on the excretion of thiamine in the urine of newborn infants indicated that only small amounts are emitted in the first few days of life.<sup>6</sup> Oral administration of thiamine by Neuweiler produced immediate excretion from the kidneys, indicative of good absorption, but giving the mother large doses of thiamine before delivery did not appreciably increase urinary excretion of this vitamin by the newborn, the placenta evidently having served as a barrier.

The total thiamine in placenta averaged 47 μg. per 100 Gm. of fresh tissue, an amount similar to those found by Taylor, Pollack, and Williams<sup>10</sup> in the stomach, testes, skin, ileum, mammary glands, ovary, and seminal ducts, but lower than were found in the heart, liver, kidney, brain, lung, spleen, and muscle. The value of 3.6 μg. per Gm. of dried material (Table I) resembles the amounts in the same tissues and also those in the adrenals and colon. Placenta contains only one-fourth to one-fifth of the amounts of thiamine in the heart and kidney, which average 18 and 14 μg. per Gm. of total solids, respectively.<sup>10</sup>

### Riboflavin

Total riboflavin per placenta averaged 820 μg. ranging from 583 to 1,480 μg. The free fraction of riboflavin averaged 296 μg. per placenta. Per 100 Gm. of fresh tissue, the averages were 151 μg. of total riboflavin and 54 μg. of free riboflavin (Table I).

Neuweiler's<sup>11</sup> total riboflavin values for seven mature placentas averaged 316 μg. per 100 Gm., within a range of 150 to 540 μg., and from the wide variations found in placentas examined at different stages of development he concluded that the riboflavin supply of the fetus is decidedly variable. He believed that since the passage of riboflavin to the fetal organism through the placenta is assumed to be dependent upon the endocrine glands, which develop markedly during pregnancy, the variation in the supply of riboflavin to the fetus might explain the avitaminotic condition observed in newborn infants. Neuweiler found the larger part of the riboflavin to be in the bound form (35 to 54 per cent) and he questioned whether the large amount of the bound fraction indicates a storage capacity of the placenta for riboflavin.

In this study, bound riboflavin averaged 64 per cent of the total riboflavin. The values per 100 Gm. of fresh placental tissue (Table I) approximate those obtained by Taylor, Pollack and Williams<sup>10</sup> for colon, testes, brain,

\*The excretion of vitamins and minerals in the urine of the infants and the mineral composition of the placentas will be reported in subsequent publications.

## PRESENT STATUS OF TRANSFUSION OF WHOLE BLOOD AND ITS DERIVATIVES IN OBSTETRICS AND GYNECOLOGY\*

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THE therapeutic value of blood transfusions is well recognized by obstetricians and gynecologists. Sudden and alarming hemorrhage is frequently encountered by them. In his analyses of maternal deaths in Brooklyn, Gordon<sup>1</sup> found that hemorrhage has been the most frequent, and so the most important cause of maternal deaths for the past ten years. In view of these facts and of recent technical advances in the field of blood therapy, and because of certain safeguards that are peculiarly essential for transfusing women potentially capable of pregnancy, a review of the status of blood transfusion as it concerns obstetrics and gynecology seems important at this time.

A decade ago blood transfusion was considered a major surgical procedure. Today, transfusions are routinely given by the house staff. It is conceded that with modern methods the actual transfusion of blood requires little training, particularly since indirect transfusions are the procedure of choice. Nevertheless, the selection of the proper blood to be administered to a particular patient requires considerable knowledge. Such responsibility cannot be delegated entirely to the laboratory, but must be borne by the attending physician also. This entails knowledge of the proper method for the collection, preservation, and administration of blood, as well as various tests for blood groupings, Rh factor, and crossmatching, and the awareness that the transfusion of some blood or plasma may result in antibody formation causing subsequent difficulties.

As a result of the tremendous experience gained during the recent war, the closed system vacuum technique for the collection, storage, and administration of whole blood is recognized as the ideal and safest method for transfusions.<sup>2</sup> Blood is drawn, stored, and dispensed in vacuum bottles. The technique is as simple and foolproof as present-day knowledge can insure. The vacuum technique practically assures absence of bacterial contamination and, if the tubing and needles used are properly cleaned, the occurrence of pyrogenic reactions can be reduced to a minimum. Until recently, 4 per cent sodium citrate solution has been used as the anticoagulant and preservative for the usual indirect transfusion. Blood stored in this medium is satisfactory for use for about five to seven days. Since in the future "bank" blood will largely be used, a preserving solution of longer effectiveness is required. Of the various solutions available at present, ACD solution, which is a mixture of citric acid, sodium citrate, and dextrose, is the most satisfactory. This solution will adequately preserve whole blood, when stored at 4° C., for twenty-one days after collection.

The recognition that proper replacement of blood loss by whole blood is essential in the therapy of hemorrhage renders inadequate most of the present-

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### Discussion

In comparison with values reported by Taylor, Pollack, and Williams for other tissues, niacin is the only one of the B vitamins considered here which is present in relatively large amounts.

Some relationships of the B vitamins in the placenta to each other and to the energy value are shown in Table II. Thiamine per 1,000 calories averaged 0.7 mg., which is more than was found in diets shown to be adequate for lactating women.<sup>12</sup> However, on the basis of calories not fat they are quite similar, that of placenta being 0.75 mg., while the diet contained 0.8 mg. per 1,000 calories.<sup>13</sup> The ratio of thiamine to riboflavin in placenta was 0.31; that of the diets of lactating women, 0.39. In studies<sup>12</sup> on human milk the thiamine to riboflavin ratio was found to be 0.36.<sup>5-7</sup> In comparing the ratio in placenta with ratios calculated from values in the literature<sup>10</sup> for human tissues, similarity was found to those for heart, testes, and skin. In placenta, riboflavin averaged 2.2 mmg. per 1,000 calories, which is greater than the amount found in the diets of lactating women, 1.07 mmg.<sup>12</sup>

The ratio of thiamine to niacin in placenta was 0.02 to 1, which is much lower than that for the diet of lactating women, 0.07 to 1,<sup>12</sup> or that of human milk, 0.08 to 1.<sup>2-3</sup> The ratio in placenta is lower than that in any of the tissues reported,<sup>10</sup> but approaches those for muscle, stomach, and ovary. In the ratios for thiamine to riboflavin and for thiamine to niacin, the placenta does not resemble closely any other human tissue for which values have been reported.

### Summary

For nine human placentas the average fresh weight was 583 Gm., the dry weight was 72 Gm. The average content of total thiamine was 256 micrograms; of free thiamine, 84 mmg.; total riboflavin, 820 mmg.; free riboflavin, 296 mmg.; niacin, 1.99 mg.; pantothenic acid, 1,535 mmg.; firmly bound biotin, 8.9 mmg.; and of loosely bound biotin, 2.0 mmg. Per 100 Gm. of fresh weight the average content was: total thiamine, 47 mmg.; free thiamine 15 mmg.; total riboflavin, 151 mg.; free riboflavin, 54 mmg.; niacin, 1.99 mg.; pantothenic acid, 279 mmg.; firmly bound biotin, 1.6 mmg.; and loosely bound biotin, 0.4 mmg.

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The obstetrician's responsibility does not end with mere determination of the patient's Rh type. If a pregnant woman is Rh negative, the blood of her husband and children, if any, should be tested also, and a careful history taken of any previous pregnancies and transfusions. When the husband is Rh positive, and there is a history of stillbirths or children with congenital hemolytic anemia, or of previous blood having been administered, either intravenously or intramuscularly, careful tests should be made for the presence of Rh antibodies. These should include the conglutination method of Wiener<sup>7</sup>; since the usual technique will not detect blocking antibodies. The tests are delicate but accurate, and should be repeated periodically during the pregnancy, especially after the seventh month. When these antibodies have been found, it is the obstetrician's duty to notify the pediatrician and to have Rh-negative blood available for both mother and child. Cases of congenital hemolytic disease should be transfused with Rh-negative blood as soon as anemia develops. If other Rh-negative blood is not available, a saline suspension of the maternal red cells which have been washed to remove the Rh antibodies may be used satisfactorily.

Recently, Polayes<sup>8</sup> and others<sup>9, 10</sup> have found that incompatibility between the A and B blood factors may also be the cause of congenital hemolytic anemia. A high titer of anti A or anti B agglutinins in a mother with a group A, B, or AB fetus may cause this condition. It follows, therefore, that stimulation of antibodies causing an increase in the titer of anti A or anti B agglutinins is to be avoided in females capable of childbearing, as a subsequent pregnancy may result in an infant with congenital hemolytic anemia. Such stimulation may be brought about by the administration of pooled plasma, the injection of incompatible whole blood, a practice once commonly employed in infants, and by the parenteral use of any solution containing group specific substances A and B.<sup>11</sup>

It is not sufficient that adequate supplies of whole blood of the various groups are on hand. Provision must be made for emergency transfusions. The admission to obstetric and gynecologic wards of women suffering from hemorrhage and shock due to placenta previa, abruptio placenta, ruptured ectopic pregnancy, and incomplete abortion, to mention a few, is a daily occurrence. Unexpected and alarming hemorrhage in the delivery room and on the wards is not uncommon. Proper treatment demands immediate replacement of blood. Even when the patient's blood group and Rh status is known, accurate cross-matching tests require time, and the resulting delay may be detrimental to the patient. While such tests are being made, "universal donor" Rh negative group O blood, with a low titer of iso-agglutinins, should be given at once and continued until properly matched blood is available.<sup>12</sup> The indiscriminate use of random group O blood as universal donor blood is condemned, as such blood may contain a high titer of iso-agglutinins and cause a severe hemolytic reaction. Group O blood in which the agglutinin titer has been reduced by the addition of group specific substances A and B is not recommended for use in women potentially capable of pregnancy, because these substances may cause increased iso-antibody formation as previously noted.<sup>11</sup>

During the emergency treatment of shock and hemorrhage, it is often impossible to insert a needle into the patient's collapsed veins. In such instances

day methods of procuring blood donations. It is estimated conservatively that four pints of blood per bed per year are required to meet minimum transfusion demands.<sup>3</sup> Unofficial surveys indicate that few, if any, of the hospitals in the United States can constantly maintain an adequate supply. Hospital blood banks, which usually exist through the solicitation of donors by the patient and the physician, are finding it difficult, if not impossible, to meet their needs. Recently, the American Red Cross, as a result of experience with its plasma and whole blood program, has announced its willingness to participate with the medical profession in a community project for the procurement of blood. This comprehensive plan calls for a community blood bank in the cities and larger towns to supply all hospitals in the vicinity with blood at no cost to the hospital or patient. In smaller communities with one or two hospitals, the Red Cross will act as a procurement agency for the hospital blood bank under the same no cost policy. These plans are actually in operation in a few localities, and need only the request and support of the medical profession for their establishment elsewhere. Thus, all blood procurement problems should be solved completely and satisfactorily.

Indications for the transfusion of blood are well accepted. Briefly, it may be stated that cases of hemorrhage and shock associated with hemorrhage should be treated with whole blood. Shock not accompanied by blood loss should have plasma infusion. Patients with anemia may be treated with whole blood or with red cell suspensions.

The proper transfusion of whole blood requires the administration of not only group compatible, but also Rh compatible blood. Of paramount importance to the obstetrician and gynecologist is the fact that whenever a transfusion is given to a woman potentially capable of childbearing, a double responsibility rests on the physician. He must be certain to give blood that will cause no immediate reaction. He must also take care not to stimulate isoantibody formation which may result in future difficulties for the pregnant woman and her fetus.

The role played by the Rh factor in the etiology of congenital hemolytic anemia and of transfusion reactions is well known.<sup>4,5</sup> Rh-negative women may become sensitized to the Rh factor and develop Rh antibodies in two ways. They may develop these antibodies as the result of carrying an Rh-positive child, or they may have been transfused with Rh-positive blood, causing the subsequent formation of Rh antibodies. Hence, determination of the Rh status in all obstetric patients and in all patients undergoing surgery or likely to be transfused is important. A complete premarital, prenatal, and pretransfusion examination should include this procedure. Potent human anti-Rh serum is to be used for such determinations as the various animal serums have not been entirely satisfactory.<sup>6</sup> It is of vital importance that every Rh-negative woman receive Rh compatible blood. This is essential not only to protect her from a transfusion reaction, but also to avoid stimulation of Rh antibodies which may cause, in the future, congenital hemolytic anemia and subsequent transfusion reactions. There is, as a rule, no harm in administering Rh-negative blood to an Rh-positive woman. Therefore, if the Rh status of a patient to be transfused is unknown, Rh-negative blood should be administered.

apparatus. The remaining portion of the blood causing the reaction should be sent to the laboratory together with 10 c.c. of the patient's freshly drawn blood and the first specimen of urine voided. Careful grouping and cross-matching tests should be performed again. The patient's blood is examined for increased bilirubin content, and the urine for hemoglobin and increased urobilinogen. The presence of hemoglobinuria or an increased bilirubinemia is definite evidence of a hemolytic reaction.

Pyrogenic reactions require no therapy other than symptomatic. Allergic reactions respond well to small doses of epinephrine. The treatment of hemolytic reactions consists in the transfusion of compatible blood and glucose and saline infusions. There is no evidence to support the theory that alkalinization of patients prior to transfusion will prevent the occurrence of reactions or lessen their severity.

When whole blood is available, the use of blood plasma in obstetrics and gynecology should be restricted to the treatment of shock without hemorrhage. Lacking whole blood, blood plasma is invaluable for the emergency treatment of hemorrhage and should be transfused until whole blood can be given. As previously mentioned, recent investigations have presented evidence that the administration of pooled plasma to females potentially capable of childbearing may cause congenital hemolytic anemia in subsequent pregnancies. This is predicated on the following facts. Pooled plasma is usually obtained from the bloods of all four blood groups, and hence will contain both A and B factors. These A and B factors are capable of stimulating the increased formation of iso-agglutinins, if administered to persons of blood group A, B, or O. A high titer of maternal iso-agglutinins can cause congenital hemolytic anemia in a fetus of a different blood group. For example, a group A fetus may have congenital hemolytic anemia caused by a high titer of anti A iso-agglutinins in its group O mother. Hence, the use of any substance which can increase the iso-agglutinin titer of women potentially capable of pregnancy is to be avoided. Therefore, the use of blood plasma in such women should be restricted to group compatible plasma. Group O plasma with a low titer of iso-agglutinins is also acceptable, since it does not contain the A or B factors.

It is granted that there is only a small possibility of such complications occurring following the use of pooled plasma. Certainly until more ample supplies of whole blood and plasma are available to permit the use of compatible plasma, no one should hesitate to administer pooled plasma when indicated.

Reactions following plasma transfusions are similar to those occurring after the administration of whole blood, although there is only a slight possibility of hemolytic reactions due to plasma. Plasma does not contain red cells, at least in significant quantities. Hence, there is no danger of a reaction caused by hemolysis of donor cells by recipient's serum. This is the major cause of hemolytic reactions. However, a plasma with a high titer of anti A or anti B iso-agglutinins can cause very serious hemolytic reactions, if given to an incompatible recipient.<sup>12</sup> This is the reason why plasma is pooled from all the blood groups. Properly pooled plasma, because of its low iso-agglutinin titer, will not cause a hemolytic reaction.

transfusion by the intrasternal route or via the femoral vein is as feasible and efficacious as the usual technique. Both of these methods have been found to be satisfactory in the treatment of severe battlefield casualties. Another point to be remembered is that the proper management of hemorrhage requires adequate replacement of the blood lost. A pint of blood given to a woman who has lost 1,500 c.c. may have little effect beyond a false sense of security to the attending physician. The amount of blood transfused should at least equal the amount lost. The speed of transfusion may also be quite important in emergency cases. There is no reason in such instances why blood may not be given by several routes at the same time. The rate of the usual transfusion should be between fifty and sixty drops a minute, but for severe hemorrhage and shock, blood should be transfused as quickly as possible and under pressure if necessary.

Blood transfusions are not without danger. Severe and fatal reactions may occur following their use. However, serious complications are invariably due to improper or imperfect technique. Reactions following whole blood transfusions may be classified into three main groups: (1) pyrogenic or thermal, (2) hemolytic, and (3) allergic.

Pyrogenic or thermal reactions are characterized by chill and fever occurring during or shortly after the transfusion. They are caused by the presence of either foreign substances or toxic products of bacterial growth called pyrogens, as the result of improper preparation of the preserving solution or of the tubing and needles used during the collection and administration of the blood. This type of reaction can be entirely eliminated by strict adherence to a pyrogen-free technique.<sup>7</sup>

Hemolytic reactions are caused by the administration of either group or Rh incompatible blood, and may occasionally be due to rare iso-agglutinins such as anti Hr and anti M. They are usually described as consisting of chill, fever, pain in the lumbar region, hemoglobinuria, and, if severe, oliguria, anuria, and subsequent death. Recent experiments have demonstrated that the clinical symptoms of chill, fever, and lumbar pain are present in less than 50 per cent of severe hemolytic reactions.<sup>12</sup> Their absence, therefore, does not preclude such a complication. Hemoglobinuria and an increased bilirubinemia are constant findings in this type of reaction. The first post-transfusion specimen of urine should be examined routinely for hemoglobin. Careful attention to grouping and crossmatching tests prior to transfusion will prevent most, if not all, hemolytic reactions.

Allergic reactions are manifested as a rule by urticaria of varying degree and severity. Occasionally, asthmatic attacks may follow transfusions. True anaphylactic shock is very rare. At the present stage of knowledge, allergic reactions cannot be eliminated. However, the use of donors who have fasted for several hours prior to their blood donation and who do not have a history of severe allergy may reduce the incidence of such reactions.

In a well-organized and properly conducted transfusion service, the reaction rate will not exceed 2 per cent. These will be mainly of the allergic type, with a few pyrogenic in nature. Hemolytic reactions should not occur.

When a reaction of any severity occurs, the transfusion should be stopped immediately, and another bottle of compatible blood given with fresh transfusion

## THE ANTEPARTUM PREDICTION OF HEMOLYTIC DISEASE OF THE NEWBORN\*

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DESPITE the intensive researches on the relationship of erythroblastosis fetalis to the Rh factor, the obstetrician is handicapped because he is unable to forecast the outcome of pregnancy in Rh-negative women. Not only is he in doubt about the presence or absence of erythroblastosis fetalis in utero, but he is also unable to predict its gravity when there are reasonable clinical indications that it may exist. As will be shown in a separate communication,<sup>1</sup> the mere existence of either anti-Rh agglutinins or "blocking antibodies" in the maternal serum antepartum—whether these substances increase, decrease, or disappear—is not necessarily correlated with the existence of hemolytic disease of the newborn, nor with its severity.

The present study is confined to an analysis of an apparent correlation between the duration of exposure of the fetus to maternal Rh antibodies and the prognosis for the newborn child. Inspection of these data discloses a partial answer to the obstetrician's dilemma. The material subjected to analysis was selected from a sample of over 4,000 pregnant women seen in the obstetric clinic of the University of California Hospital and in the private practices of six obstetricians, who submitted regular antepartum blood samples for study. The blood serum from each patient was tested for agglutinating antibodies against two Rh negative group O, and two Rh positive group O red blood corpuscle suspensions. The presence of blocking antibodies was determined by the method of Wiener.<sup>2</sup>

In the majority of instances, the first blood sample was not obtained until the third trimester of pregnancy. Thus, when antibodies were found at this time, it was impossible to know when they had first appeared. The appearance time, however, could be dated in 26 cases, and it was immediately apparent that no cases of erythroblastosis occurred when the antepartum duration of antibodies was ten weeks or less. In all cases, the "appearance time" was estimated to be midway between the time of the last negative sample and the time of the first positive sample. In the remaining material, it was therefore logical to exclude all cases in which the first blood sample had been obtained less than ten weeks before delivery, but to include those in which the first positive sample was obtained "more than eleven weeks" or "more than sixteen weeks," et cetera, before parturition.

After such exclusion, 49 cases remained for analysis. By inspection, it was noted that in 19, only "traces" of either agglutinating or blocking antibodies had been found, or there had been an isolated finding of a small ("one plus"

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Human albumin, a product of the fractionation of whole blood, is of little interest to the obstetrician and the gynecologist. It may be used occasionally in pernicious vomiting of pregnancy, hypoproteinemia, nephrosis, and debilitated states. However, in all of these instances amino acid preparations are more effective when intravenous protein therapy is indicated.

The various preparations offered as substitutes for whole blood and human plasma, including bovine albumin, gelatin, sodium arabinates, peetin, and isinglass have not been found satisfactory, and some are actually harmful. An ample supply of whole blood and plasma will make their use unnecessary.

Red-cell suspensions are useful in the treatment of anemias. These suspensions are usually obtained as a by-product of the processing of whole blood for plasma. Since the Army and Navy have recently released a large supply of blood plasma to civilian hospitals, less blood will need to be converted into plasma. This will reduce the amount of red-cell suspensions available. It will, therefore, be more practical to use whole blood for the therapy of anemias.

### Summary

Blood transfusions are an essential form of obstetric and gynecologic therapy. In view of the recent advances in the knowledge of this subject, obstetricians and gynecologists have a definite threefold responsibility: (1) To have an ample supply of whole blood and plasma available. This can be assured by the establishment of a community blood bank such as suggested by the Red Cross. (2) To demand that the collection, preservation, and administration of whole blood and plasma conform to the best technical standards. The adoption of the closed system vacuum technique and the use of the ACD preserving solution will meet such criteria. (3) To insure that blood or plasma administered to their patients must be beneficial without reaction, and to avoid antibody stimulation which may subsequently cause difficulties in later pregnancies or transfusions. This can be accomplished under a pyrogen-free technique by the use of group and Rh compatible blood for routine transfusions, of Rh-negative group O blood with a low titer of iso-agglutinins for emergency transfusions, and of group compatible or group O plasma with a low iso-agglutinin titer when plasma is indicated.

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Rh antibodies first appear less than ten weeks from term, and probably useless when they appear more than fifteen weeks from the time selected for induction of labor. The termination of pregnancy by conservative means and prompt transfusion\* of the anemic child at birth should result in a higher survival of infants only in that small group of mothers wherein antibodies appear for the first time ten to sixteen weeks before the estimated date of confinement. Beyond that period, any attempt to reduce the exposure to ten weeks or less would probably result in the loss of the child from prematurity, or from a combination of prematurity and erythroblastosis. Eleven of the cases included in this study were primigravid women, and in all but one the antibodies appeared late in pregnancy, which probably explains why first babies characteristically, but not invariably, escape the disease.

These findings may be summarized and translated into tentative suggestions for the management of obstetric patients as follows:

Ideally, all pregnant women should be typed routinely, regardless of parity, and in those Rh-negative patients having Rh-positive husbands, the first sample of blood for antibody determination should be obtained not later than the twenty-fourth week of pregnancy. If this be strongly positive for either agglutinating or blocking antibodies, an Rh-positive fetus will probably be too seriously affected by hemolytic disease to warrant any interference before term, while an Rh-negative fetus will escape the disease. As yet, there is no way to distinguish these possibilities except to prove that the father is homozygous for the Rh factor. If the antibodies are present only in "traaces," or if a small amount is found on a single determination and is unconfirmed by subsequent tests, the fetus is probably unaffected, and again it would be unwise to interfere.

If the initial sample is free of antibodies, but a significant amount appears later, a period of eight to ten weeks may be allowed to pass before hemolytic disease becomes a probability. After this time, induction of labor might be warranted providing the expected date of confinement is within the ensuing six weeks.

That a relationship exists between the duration of exposure to maternal antibodies and the fetal prognosis seems apparent. Further study may alter the critical time periods established by the data of this preliminary analysis.

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\*It is recommended that an immediate slow transfusion of 50 to 75 c.c. of Rh-negative group O blood be given into the umbilical vein.

or "partial") amount of either type of antibody which was unconfirmed by subsequent and repeated tests. Only one case of possible erythroblastosis fetalis occurred in this group, that of a baby who had a slight increase in the number of nucleated red blood cells at birth, and who suffered from a mild anemia which did not require transfusions.

In the remaining 30 cases, appreciable amounts of antibodies were found, or small amounts were present on repeated occasions. In 22 of these cases, the antibodies appeared more than ten weeks before delivery, and all 16 cases of erythroblastosis fetalis were found in this group. The remaining six women were delivered of normal infants, four of whom proved to be Rh-negative children of mothers who had been previously sensitized, and presumably this pregnancy had elicited a nonspecific anamnestic recall of Rh antibodies. Unfortunately, there was no way of differentiating antepartum the mothers of these four cases from those who were carrying Rh-positive infants. The remaining two exceptions cannot be explained.

TABLE I. THE RELATIONSHIP OF THE APPEARANCE TIME OF RH ANTIBODIES BEFORE DELIVERY TO THE OCCURRENCE AND SEVERITY OF HEMOLYTIC DISEASE OF THE NEWBORN

ANTIBODY APPEAR- ANCE (NO. WEEKS ANTEPARTUM)	CASES WITH "TRACES" OR AN ISOLATED SMALL AMOUNT OF ANTI-RH OR BLOCKING SUBSTANCE	CASES WITH LARGER AMOUNTS OF ANTIBODIES, OR WITH SMALL AMOUNTS WHICH WERE REPEATEDLY CONFIRMED*	
1 to 9	8—All normal	Rh+ infants 7—All normal	Rh- infants 1—normal
10 to 14	3—All normal	8 { 1 normal 3 "subclinical" 4 icterus gravis (3 deaths)	2—Both normal
15 to 36	8 { 7 normal 1 questionable "subclinical"	10 { 1 normal 1 hemolytic anemia 1 icterus gravis 7 hydrops fetalis (7 deaths)	2—Both normal

\*Cases with positive antibodies on first samples obtained less than ten weeks before delivery were excluded (see text).

The results of classifying these cases as described are summarized in Table I. The influence of the appearance time of antibodies upon the prognosis is further emphasized when the ten- to fourteen-week period is studied separately from the fifteen- to thirty-six-week period. Hemolytic disease of the newborn varies in its severity from the mildest subclinical variety through the simple, though often severe, anemia to the "icterus gravis" form, in which there is widespread pigment deposition at birth, and finally to the universally fatal "hydrops fetalis" with its widespread visceral damage and generalized edema. All of the mild (subclinical) cases occurred in the ten- to fourteen-week group. Of the eight Rh-positive babies in this group, seven had hemolytic disease, and of these, three died of icterus gravis. On the other hand, *all seven cases of fatal hydrops fetalis were found in the 10 Rh positive infants of the group in which maternal antibodies had appeared at least fifteen weeks or more before the delivery.*

If such figures as these are confirmed by subsequent study of a larger series, it becomes obvious that the induction of premature labor is unnecessary when



technique. Two applicators were used on each infant, the first of which was placed immediately in sodium azide broth, while the second applicator was used to streak MacConkey's agar and Sabouraud's glucose agar plates.

In the first series of 100 unselected newborn infants, a specific attempt was made by the use of selective media to isolate staphylococci, coliform bacilli, and moniliae. The staphylococci were isolated according to the method of Pike.<sup>6</sup> Sodium azide blood enrichment broth was inoculated by placing the oronasal swab in the broth and incubating twenty-four hours at 37° C. Brain and heart infusion blood agar was streaked from this broth, incubated overnight at 37° C., and any hemolytic staphylococci picked and tested for coagulase activity. Coliform organisms were determined by direct streaking of MacConkey's medium with the oronasal swab and incubating at 37° C. for twenty-four hours. Yeast-like fungi were found by direct streaking of Sabouraud's glucose agar with the oronasal swab and incubating at 37° C. for a period of seven days. *Candida albicans* strains were identified by the formation of chlamydospores on corn meal agar together with their fermentation reactions in glucose, maltose, sucrose, and lactose broths. All yeasts not producing mycelia in corn meal agar were tested for ascospore formation on potato glucose agar.

A second series of 50 unselected newborn infants was studied with special reference to streptococci and pneumococci. Approximately 0.5 ml. of aspirated material from the newborn infant's oral and nasal cavities was placed in a sterile test tube. At the same time, an oronasal swab was placed in sodium azide crystal-violet blood enrichment broth devised by Pike<sup>6</sup> for streptococci and incubated overnight at 37° C. Brain heart infusion blood agar plates were streaked from this enrichment broth, incubated twenty-four hours at 37° C., and examined for alpha and beta hemolytic streptococci.

The aspirated material in each test tube was injected intraperitoneally into a mouse for the detection of pneumococci. All mice living at the end of twenty-four hours were sacrificed, and a swab of the abdominal cavity streaked on brain heart infusion blood agar. After incubation at 37° C. for twenty-four hours, colonies showing alpha hemolysis were examined for pneumococci.

TABLE I. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO LENGTH OF TIME MEMBRANES WERE RUPTURED BEFORE BIRTH

DELIVERIES*		STAPHYLOCOCCI	COLIFORM	MONILIAE
NUMBER	PER CENT			
<i>Membranes Ruptured 1 to 12 Hours</i>				
38	42.0	-	-	-
30	33.0	+	-	-
10	11.0	-	+	-
4	4.4	+	+	-
4	4.4	-	-	+
2	2.2	-	+	+
2	2.2	+	-	+
1	1.0	+	+	+
<i>Membranes Ruptured 12 to 24 Hours</i>				
1	16.6	-	-	-
3	50.0	+	-	-
1	16.6	-	+	-
1	16.6	+	+	-
<i>Membranes Ruptured 24 to 72 Hours</i>				
1	33.3	+	+	-
1	33.3	+	-	+
1	33.3	+	+	+

\*Afebrile patients.

# BACTERIOLOGY OF THE ORONASAL CAVITY OF THE NEWBORN

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**A** KNOWLEDGE of the organisms that are found in the oronasal cavity of the newborn under routine conditions of labor and delivery in a hospital is of great practical importance to the clinician. It furnishes information relative to the organisms normally present under these circumstances, so that their relationship as secondary invaders to a primary infection can be better understood. It also sheds light on the types of organisms which frequently contaminate the newborn during labor and delivery and their probable source.

Some information on this problem is afforded by the results obtained by other investigators on studies of the bacterial flora of the human vagina, skin, and rectum. Of major importance is the question of whether puerperal infections are intrinsic or extrinsic in origin, and likewise whether infections of the newborn child are obtained from the mother or are extrinsic in origin.

Lancefield and Hare<sup>1</sup> examined by the precipitin test a large number of hemolytic streptococci which had been obtained from women suffering from puerperal infections and from women with afebrile puerperia. Forty-five out of 46 strains isolated from puerperal fever cases fell into Lancefield's Group A, while only one out of 65 strains isolated during afebrile puerperia was *Streptococcus pyogenes*. Of 13 strains isolated from vaginas before labor, none was *Str. pyogenes*. Colebrook, Maxted, and Johns<sup>2</sup> failed to detect *Str. pyogenes* on the perineal or perianal skin of 160 women during pregnancy, while Hare and Maxted<sup>3</sup> failed to isolate *Str. pyogenes* from the feces of 100 normal women during the first stage of labor.

In 1938, Weinstein<sup>4</sup> published a critical report on the bacterial flora of the human vagina under varying conditions of disease and of pregnancy. Of 375 patients examined, staphylococci were isolated 254 times. Eleven were hemolytic *Staphylococcus aureus* isolated from pregnant women who subsequently suffered no complications at parturition or in the puerperium. Hemolytic streptococci were isolated 29 times, but no effort was made to type them. *Escherichia coli* was found to be present in only 27 of the cases studied, which refutes the common belief that it is a frequent inhabitant of the vaginal tract. No appreciable difference could be detected in the flora obtained from pregnant, non-pregnant, or in healthy and diseased genital tracts.

Carter and his associates<sup>5</sup> cultured the yeastlike fungi from the vagina and vulvas of 200 pregnant women and found an incidence of 86 positives for these fungi, of which 20 were classified as *Candida albicans*.

## Materials and Methods

Immediately following delivery, before the oral and nasal cavities of the infants had been aspirated of mucus, sterile cotton applicators were directed into the posterior oronasal pharynx and nasal orifices, using careful aseptic

TABLE III. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO LENGTH OF TIME MEMBRANES WERE RUPTURED BEFORE BIRTH, SECOND SERIES

DELIVERIES*		STREPTOCOCCI	PNEUMOCOCCI
NUMBER	PER CENT		
<i>Membranes Ruptured 1 to 12 Hours</i>			
35	85.0	-	-
5	12.5	alpha +	-
1	2.5	beta +	-
<i>Membranes Ruptured 12 to 48 Hours</i>			
5	55.5	-	-
1	11.0	alpha +	-
3	33.5	beta +	-

\*Afebrile deliveries.

C. and were not killed by heating at 60° C. for thirty minutes. From these results it was concluded that these organisms belonged to the enterococcus group of streptococci, *Streptococcus fecalis*. (Group D antiserum unavailable.)

According to Table III, a predominance of beta streptococci (33.5 per cent) were present when the membranes had been ruptured twelve to forty-eight hours, as compared to 2.5 per cent for the shorter period of one to twelve hours. There were also a predominance of beta streptococci (11 per cent) present, Table IV, when delivery was by low forceps, as compared to no beta streptococci in the spontaneous deliveries. In this series, there were 13 spontaneous, four low forceps, and 33 elective low forceps deliveries. There were no mid-forceps, cesarean sections, or febrile patients.

Special mention should be made here of three patients in the first 100 series who were febrile intrapartum, Table V. Two of the infants had positive staphylococci cultures, while the other had a positive coliform culture.

TABLE IV. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO TYPE OF DELIVERY, SECOND SERIES

DELIVERIES*		STREPTOCOCCI	PNEUMOCOCCI
NUMBER	PER CENT		
<i>Spontaneous Deliveries</i>			
11	85.0	-	-
2	15.0	alpha +	-
0	0	beta +	-
<i>Low Forceps Deliveries</i>			
29	78.0	-	-
4	11.0	alpha +	-
4	11.0	beta +	-

\*Afebrile deliveries.

TABLE V. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WHOSE MOTHERS HAD INTRAPARTUM FEVERS

<i>Febrile Patients</i>			
NO. OF DELIVERIES	STAPHYLOCOCCI	COLIFORM	MONILIAE
1	-	+	-
2	+	-	-

### Discussion

These 150 oronasal cultures were obtained from consecutive deliveries in a private institution staffed by both the general practitioner and specialist. No effort was made to change the labor or delivery care of these patients by the

## Findings and Results

Thirty-nine of the first series of 100 cultures from newborn infants were negative for staphylococci, coliform bacilli, and moniliae, Table I. Forty-four strains of hemolytic staphylococci were isolated, two of which were coagulase positive. Twenty-one plates positive for coliform organisms were found, with 11 of them showing the cultural characteristics for *E. coli*. Of the 11 yeast strains isolated, only two were *Candida albicans*.

All three deliveries in which the membranes had ruptured twenty-four to seventy-two hours prior to delivery showed positive cultures in the infants for staphylococci, coliform bacilli, or streptococci (Table I). There were 83 per cent positive cultures for six infants in which the mother's membranes had been ruptured twelve to twenty-four hours prior to delivery, while only 58 per cent of 91 infants had positive cultures when the mother's membranes had been ruptured one to twelve hours before delivery.

There were two neonatal deaths which at autopsy yielded reports of atelectasis and subdural hemorrhage, and cerebral hemorrhage, respectively.

There were 22 spontaneous, 55 elective low forceps, 19 low forceps, two midforceps, and two elective cesarean section deliveries.

TABLE II. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO TYPE OF DELIVERY

DELIVERIES*		STAPHYLOCOCCI	COLIFORM	MONILIAE
NUMBER	PER CENT			
<i>Spontaneous Deliveries</i>				
8	36.4	-	-	-
6	27.3	+	-	-
3	13.6	-	+	-
2	9.1	+	+	-
2	9.1	-	-	+
1	4.5	-	+	+
<i>Low Forceps Deliveries</i>				
29	39.2	-	-	-
25	33.8	+	-	-
8	10.8	-	+	-
4	5.4	+	+	-
2	2.7	-	-	+
1	1.4	-	+	+
3	4.0	+	-	+
2	2.7	+	+	+
<i>Midforceps Deliveries</i>				
2	100.0	+	-	-
<i>Cesarean Section Deliveries</i>				
2	100.0	-	-	-

\*Afebrile patients.

According to Table II, 64 per cent of the infants' oronasal cavities yielded positive cultures for staphylococci, coliform, or moniliae when delivery occurred spontaneously, as compared to 61 per cent positive cultures when delivery was by low forceps. The two midforceps cases gave positive cultures for staphylococci, while two cesarean sections were negative for the three organisms studied.

In the second series of 50 cases, Table III, only streptococci and pneumococci were investigated. Pneumococci were not found by the methods used. However, six cases yielded alpha streptococci, and from four other cases beta streptococci were isolated. The beta strains were tested by Lancefield's precipitin reaction and found to be negative with groups A, B, and C antisera. All strains of streptococci including both alpha and beta were able to grow at 45°

### Conclusions

1. The oronasal cavity of the newborn has been found to contain staphylococci, the enterococcus group of streptococci (*Str. fecalis*) and moniliae in approximately the same ratio as other investigators have found them to be present in the vaginal tract of the pregnant woman. On the other hand, a much higher percentage of *E. coli* organisms were present in the infant's oronasal cavity than previously reported for the pregnant vagina, which is presumed to represent contamination from the rectum in labor or during delivery.

2. A definite correlation was observed between the length of time the membranes had been ruptured and the frequency with which organisms were found in the oronasal cavity of the child. A larger percentage of infants were contaminated during longer than during shorter labors.

3. Pneumococci were not found in these cases, nor were streptococci of the puerperal fever type found. Only two of the 44 strains of staphylococci were coagulase positive. Eleven yeastlike fungi were isolated of which two gave the true characteristics of *Candida albicans*.

The authors wish to express their appreciation to the medical staff of St. Joseph's Maternity for its wholehearted cooperation in making all their patients available for inclusion in this study, and also to the nursing and record room staffs for their helpful assistance.

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attending physicians for this series, thus the results comprise a representative cross section of obstetric practice under the labor and delivery circumstances of this institution.

Only one case had been given chemotherapy prior to delivery. This patient was a severe pre-eclamptic whose membranes had been ruptured twenty hours prior to delivery. Even though she was afebrile, 1 Gm. of sulfadiazine was orally administered prophylactically. Bacteriologic cultures of this newborn's oronasal cavity yielded coagulase positive staphylococci and coliform bacilli.

In Table I, the bacteriologic data from the first series of 100 deliveries was arranged according to the length of time the membranes had been ruptured. There was a marked increase in the percentage of positive cultures obtained when the membranes had been ruptured a long time as compared to the shorter periods. This percentage ranged from 42 per cent for the shorter interval of one to twelve hours to 100 per cent in the longer period of twenty-four to seventy-two hours. This observation should be of significance to the obstetrician.

In Table II, the above data from the first 100 deliveries was rearranged to correlate bacteriologic results with types of deliveries. A study of this table reveals no significant differences between the use of low forceps and the occurrence of spontaneous deliveries. Midforceps were used in only two cases, which is too small a number from which to draw any conclusion.

The results obtained in the search for pneumococci and streptococci suggest that streptococci causing puerperal fever are probably extrinsic in origin and also that pneumococci capable of infecting the infant are not normal inhabitants of the vagina.

There was a larger percentage of beta streptococci present when the membranes had been ruptured a long time or whenever forceps were used. However, the small number of streptococci found does not give these results significance.

Weinstein<sup>4</sup> found the vaginal flora to contain staphylococci in 67 per cent and beta-hemolytic streptococci in 8 per cent of the 375 women studied, while the results of this study showed 44 per cent positive for staphylococci (first series) and 8 per cent for beta-hemolytic streptococci (second series).

Moniliae of the *Candida albicans* type are not infrequently found in the vaginas of pregnant women and they may or may not have clinical importance. In this series from 100 oronasal cultures, eleven yeastlike fungi were isolated of which two were classified as *Candida albicans*. Thus, two infants had *Candida albicans* present in their oronasal cavities, but which showed no clinical signs of thrush.

*E. coli* were present in a larger percentage of cases than would have been expected on the basis of other work. These bacteria were found in 11 per cent of this series, while Weinstein<sup>4</sup> recorded only 6 per cent. The high incidence of *E. coli* organisms was undoubtedly due to fecal contamination during parturition.

It is also of cogent interest to point out here that according to our results it is possible to have deliveries which show a minimum contamination of the newborn infant's oronasal cavity.

A. *Disturbances of Menstruation*

- I. Disturbances in the regularity of the cycle
  - a. Shortened cycle (polymenorrhea)
    1. Premature interruption of the cycle
  - b. Lengthened cycle (oligomenorrhea)
    1. Persistent corpus luteum
    2. Hyperplasia of the endometrium
    3. Inhibited cycle followed by a normal cycle
  - c. Amenorrhea
    1. Physiologic
    2. Primary amenorrhea
    3. Secondary amenorrhea
  - d. Ayclic bleeding (metrorrhagia)
- II. Disturbances in the amount of menstrual flow
  - a. Profuse flow (hypermenorrhea)
    1. Hypoplastic uterus
    2. Hypothyroidism
    3. Tumors (polyps, submucous myomas)
    4. Pelvic congestion
    5. Endometrial hyperplasia
  - b. Scanty flow (hypomenorrhea)
    1. Hypogonadism
    2. Hyperthyroidism
- III. Disturbances in the duration of menstrual flow
  - a. Lengthened bleeding period (menorrhagia)
    1. Irregular shedding and irregular ripening
    2. Endometrial hyperplasia
    3. Inflammatory
    4. Tumors (benign or malignant)
  - b. Shortened bleeding period.
    1. Hypogonadism

B. *Nonmenstrual Bleeding*

- I. *Disturbances under ovarian control*
  - a. Cystic glandular hyperplasia
    1. Granulosa-cell tumors
  - b. Ovulation bleeding
  - c. Anovulatory bleeding
  - d. Following hormone treatment
- II. *Disturbances not under ovarian control*
  1. Uterine, ayclic bleeding (metrorrhagia)
    - a. Tumors (polyps, myomas)
    - b. Incomplete abortion
    - c. Infection
    - d. Malignancy
  2. Adnexal
    - a. Tumors
    - b. Pelvic inflammatory disease
  3. Blood dyscrasias
    - a. Purpura hemorrhagica
    - b. Leucemia
    - c. Aplastic anemia
  4. Constitutional diseases
    - a. Congenital syphilis
    - b. Tuberculosis

## MENORRHEAL PROBLEMS IN COLLEGE WOMEN\*

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NINETEEN thousand, two hundred and eighty-three women entered the University of Minnesota from 1935 to 1945. Of these, 5,210 women consulted the gynecologic department of the Student Health Service. Most of these were between the ages of 18 and 25 years. The three common symptoms which brought the students to this department were: pain, vaginal discharge, and irregular bleeding. One thousand, six hundred and sixty-seven women came in because of irregular bleeding, an incidence of 32 per cent. The term "menorrhea" might be used to include all of the factors associated with periodic bleeding from the uterus. The changes of the endometrium are controlled by a complex endocrine mechanism. Obviously, uterine bleeding may occur under many conditions.

Before a scientific treatment of menorrheal bleeding is possible, one must understand the physiology of menstruation. The physiologic purpose of the uterus is to house and nourish the fertilized ovum to maturity. If menstruation is to be considered a normal phenomenon, then it must be due to the change in a normal structure. It may be more satisfactory to limit the term menstruation to bleeding which occurs from an endometrium which has undergone the cycle of changes necessary for nidation, and the presence of a fertilizable ovum. All of the endocrine glands probably influence the menstrual cycle. It is dependent upon the hormones of the anterior pituitary gland, the response of the ovary, and the response of the uterus to both the pituitary and ovarian stimulation. The appearance of the ovaries and uterus may vary during successive periods in the same woman or at the same stage in different individuals.

The menstrual cycle may be divided into three phases: (1) the proliferative, estrogen, or preovulatory phase; (2) the secretory, progesterin, or post-ovulatory phase; and (3) the menstrual or dismantling phase. Some authors further divide the phases into repair phase, resting phase, and early and late secretory phases. The menstrual phase is attended by bleeding from the spiral arterioles with the exfoliation of the compacta and the spongiosa layers of the endometrium, leaving only the basal layer intact.

The literature on menorrheal irregularities is confusing because of the discrepancy of terms used. Uterine bleeding may be divided into two main categories: disturbances of menstruation, and nonmenstrual bleeding. Uterine bleeding will continue until healing by epithelization occurs. The amount of bleeding depends upon the size of the vessels involved and their resistance to closure by natural or mechanical means. A modified Schroeder classification has been used as a basis to sort out the various types of bleeding. As more information is available from hormone studies and endometrial curettings, the subdivisions of the following classification will become apparent.

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as well as sufficient rest and relaxation. Ferrous sulfate was given when the hemoglobin was below 12 Gm.; and some received Fowler's solution. The hormone assays done under the direction of Dr. Leo Samuels and the Department of Physiology after the administration of gonadotrophins showed an increase in the output of estrin in the urine but did not affect the pregnanediol levels in our series. It must be kept in mind that gonadotropic hormones might produce polycystic ovaries. The use of x-ray or radium has never been necessary to control the bleeding in any of these cases, nor has a hysterectomy been performed in any of these young women.

B. *Irregular shedding* probably represents the corpus luteum phase. The normal tempo of the flow is maintained, but the regeneration of the endometrium is prolonged. The amount of flow is variable. A diagnostic curettage between the eighth and tenth days of bleeding usually reveals the transition between the functioning phases, indicating a delay in healing. The peripheral glands are collapsed into peculiar shapes. The epithelium is in the secretory phase in part of the slide and proliferative in part. Hormone assays in irregular shedding indicate the excretion of pregnanediol continuing during the bleeding phase. Curettage alone cures about 50 per cent of these cases. Many must clear up spontaneously, because years ago I prescribed "sistomensin," moecasin snake venom, or calcium, during the bleeding phase with good results in 60 per cent of the cases. Thyroid and iodine medication also benefits this condition. Giving 1 mg. of diethylstilbestrol daily after the fifth day of bleeding and continuing for three weeks, together with 10 mg. daily of anhydro-hydroxy progesterone (pranone or pregneninolone) during the third week, has been followed by cures.

C. *Anovulatory bleeding* represents a premature interruption of the menstrual cycle. Many histories indicate painless menorrhagia the first year or two after the beginning of catamenia. Painless uterine bleeding after the administration of estrogen in the first half of the cycle are frequent, and the flow is usually not quite normal and may be early. Are these not anovulatory cycles? No treatment is indicated unless there is a sterility problem.

It may be impossible to determine whether or not ovulation has occurred. In two cases of sterility only one peak of estrin was found in hormone assays of the urine. However, there is no quantitative method to determine ovulation. When the endometrium is secretory, we assume there is a normal functioning corpus luteum. Even with serial sections of both ovaries, very few can diagnose histologically an active corpus luteum.

D. *Oligomenorrhea* or infrequent cycles is a common finding in college women. Hormone assays in two cases of oligomenorrhea revealed an increase of ketosteroids in the androgen fraction of the urine. A persistent corpus luteum may cause a decidua-like reaction of the stratum compactum of the endometrium with a delayed menstruation. Many women with a delayed period start to flow following a pelvic examination. This may be a psychic effect, or it may also be due to the fact that the examiner may have ruptured the persistent corpus luteum. To reassure the patient that she requires no therapy usually suffices.

- c. Cardiac decompensation
- d. Graves' disease
- e. Nervous disorders (shocks, fright)

A detailed history by systems and a general physical examination was done on each student before she consulted me. The examination included a general physical examination, blood serology, Mantoux test, hemoglobin, and urinalysis. A gynecologic history and a careful one-finger bimanual pelvic and/or a rectal examination was made on every woman who had gynecologic complaints. When indicated, other studies were done, including basal metabolism rate; serum cholesterol; prothrombin, bleeding and clotting time, and platelet count; erythrocyte and leucocyte count with differential; sedimentation rate; and x-ray of the sella tureica. Vaginal smears were taken with a pipette and stained according to the method of Papanicolaou, but in this age group they were not very helpful. Endometrial biopsies were not done except after a curettage had previously been performed. Parental permission for any surgical procedure is required for our college students.

Abnormal uterine bleeding may be divided into two groups: (1) disturbances of the endocrine glands, and (2) bleeding associated with constitutional diseases.

#### *I. Disturbances of the Endocrine Glands.—*

A. *Cystic glandular hyperplasia* is probably due to a dysfunction of the anterior pituitary gland with secondary ovarian failure. In hormone assays done on a patient with this condition, the estrin output in the urine was maintained at a high level. A diagnostic curettage is done when possible if hyperplasia is suspected. The typical "Swiss cheese" picture is frequently lacking. However, usually the curettings are abundant, and the glands are irregular in size and shape, and nonsecretory, indicating an exaggeration of the proliferative phase. One hundred and ten cases of hypermenorrhea and/or menorrhagia were seen. Of these, 62 improved under thyroid medication, the dose being pushed to three times the daily dose during the flow. Because of profuse flow, a diagnostic curettage was done on 24 patients with hypermenorrhea and/or menorrhagia. Ten, or 41 per cent, had less bleeding in cycles following curettage. A hyperplastic endometrium was found in 19 patients. The remainder of the endometria showed proliferative phase, secretory phase, or polypoid type. In the bleeding phase, bed rest, elevating the foot of the bed, ergot, vitamin K, and blood transfusion was given as indicated, sometimes with large doses of estrogens or anterior pituitary-like substances. After the bleeding phase, equine gonadotrophin was given as follows: intramuscular injection of 10 Cartland-Nelson units of gonadogen, then 20 Cartland-Nelson units on alternate days for a total of 90 units, and this was followed by 1,000 units of chorionic gonadotrophin on alternate days for five doses. One series of injections took care of six, or 43 per cent, more of these patients. A second series was started on the seventh to ninth day of bleeding if it was prolonged. It is important to watch for serum reactions and, therefore, the intravenous injection was given in only one case. A high vitamin diet was prescribed and strenuous exercise advised,

under anesthesia. The remaining five cases had hypoplastic uteri, with hypogonadism and normal basal metabolic rates. Four of them had periodic bleeding following the administration of estrogens, 10,000 units every other day for three weeks and 5 to 10 units of progesterone intramuscularly given concomitantly with the estrogens the third week. No treatment was given the fourth week. This regime was repeated for three successive months unless uterine bleeding occurred. The one-two method of gonadotropic hormone injections was then given. The uteri of all of these women increased in size during the treatment, and the patients developed a feeling of well-being. One woman was overweight and was given thyroid also. The menstrual period did not continue to be regular in any of these women without some stimulation six to twelve months later. However, usually stilbestrol and pranone were sufficient to bring on the bleeding once it was established. One of these students has married and has had one pregnancy. Since her pregnancy she again has an amenorrhea which has now persisted for six months, although she is not nursing her baby. One patient has never menstruated and has been advised against further endocrine therapy for the time being. She was given both types of treatment and also thyroid, the latter over a period of one year.

Secondary amenorrhea may be an early sign of dementia precox. It may also be due to constitutional causes. Physiologic amenorrhea is cared for by the patient's private physician, but a number of women come in for a diagnosis of pregnancy.

## II. *Bleeding Associated With Constitutional Disorders.*—

The underlying cause obviously is treated when examination reveals the bleeding to be due to constitutional disorders. The university students are on the whole in excellent health, and chronic ailments are but rarely encountered. Bleeding due to the following conditions has not been evident in this group.

- a. Granulosa-cell tumor of the ovary.
- b. Blood dyscrasia (purpura hemorrhagica, aplastic anemia, and acute lymphatic leucemia).
- c. Congenital or acquired syphilis.
- d. Tuberculosis.
- e. Graves' disease.
- f. Cardiac decompensation.
- g. Teratoma and sarcoma (four women had laparotomies and dermoid cysts of the ovaries were removed). Very few gynecologic laparotomies have been done on college students in the past five years because of the good economic conditions. The surgery is done by the student's private physician during the summer vacation.
- h. Polyps of the cervix are very uncommon in this group.
- i. Endocervicitis and cervicitis are treated by electrocautery, and usually one treatment suffices.
- j. Pelvic inflammatory disease is uncommon. With sulfonamides and penicillin, the few acute Neisserian infections seen have been readily cured.
- k. Malpositions of the uterus. Most of the retroversions of the uterus are apparently congenital in type and have no apparent relation to irregular bleeding.

CASE 1.—A 21-year-old student presented herself in January, 1944, because she had not become pregnant after having been married for one year. Onset of catamenia occurred at 11 years of age. Periods were regular until 1940, then they occurred every twenty to twenty-three days with one day of scanty flow. During the past year the periods had become more infrequent, skipping up to four months. General examination was negative, except that she was slightly underweight. Her basal metabolic rate was minus 23 per cent to minus 8 per cent. The patient tolerated one grain of thyroid daily. Pelvic examination was negative, except the uterus was about two-thirds normal size. The patient had a moderate flow following stilbestrol and pranone, and then was given gonadotrophin, the one-two method, with no period following. The medication was discontinued, except for thyroid for a period of one year, during which time the patient had a scanty flow for one day every month or two. In November, 1944, the patient passed a uterine endometrial cast which had decidua-like cells. Dr. Robert Meyer said it was not due to pregnancy, but probably to a persistent corpus luteum. The patient became anxious for a pregnancy, because her husband was to be inducted into the Army. Fertility studies were made, and the x-ray of the tubes revealed patency. A Huehner test was also normal. A diagnostic curettage on the first day of bleeding revealed follicular phase of the endometrium in January, 1945. An endometrial biopsy in March on the first day of bleeding was nonsecretory. The patient skipped two periods and again passed a cast of the uterus May 12, 1945, similar to the previous cast. She had a two-day period in June, 1945, and delivered a full-term baby boy in March, 1946. The conclusion was that the patient ovulated in June without medication.

E. *Amenorrhea* in college women is usually secondary and due to change of environment. It is interesting to note a case of twin girls who had regular menstrual periods until they entered college. They both stopped menstruating, and one reported to me. I suggested her returning after the Christmas vacation, if she did not have a period; both of them had normal cycles while at home, but again the periods ceased when they returned to school.

Continued amenorrhea is the cause of much concern to the student and her parents. Substitution therapy is not a cure, but bleeding may be produced with diethylstilbestrol priming and combined with oral progesterone. Whether bleeding is produced from a proliferative or secretory endometrium has the same psychic effect upon the patient. Withdrawal of ovarian hormones initiates the usual menstrual behavior of the coiled arteries. Progesterone given during the first half of the cycle produced bleeding within seventy-two hours after withdrawal. Hormone shots are expensive and annoying to the patient. Producing a menorrhoeal flow by oral medication helps to reassure the student. Following the oral administration of stilbestrol and pranone, bleeding occurs within forty-eight hours of progesterone cessation. I usually prescribe it after six months of amenorrhea. Many of the students menstruate when they are home on vacation and require no therapy. Estrogens in large doses or over a long period of time may inhibit the pituitary and reduce the ovarian function.

In the past ten years, I have examined eight cases of primary amenorrhea. Three of these had normal secondary sex characteristics with no evidence of uterus or vagina. No treatment was given except to inform the student of her condition in two cases. In the third, the mother refused this information being given to her daughter, but gave her consent for an examination of the patient

## A DIAGNOSTIC TECHNIQUE FOR THE DETECTION OF ENTEROCELE

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ENTEROCELE was formerly believed to be a surgical rarity. Considered opinion now regards its "rarity" as based on lack of detection rather than occurrence. High rectoceles and posthysterectomy rectoceles are more frequently true enteroceles, either undetected at operation or developing subsequent to (usually) supravaginal hysterectomy. Certainly it is seen too often to be considered other than a probable accompaniment of marked rectocele, or the sole cause for the posterior vaginal wall bulge when the latter extends high in the vagina. While gynecologists may be concerned with its existence and treatment, its nature and even name are foreign to most practitioners.

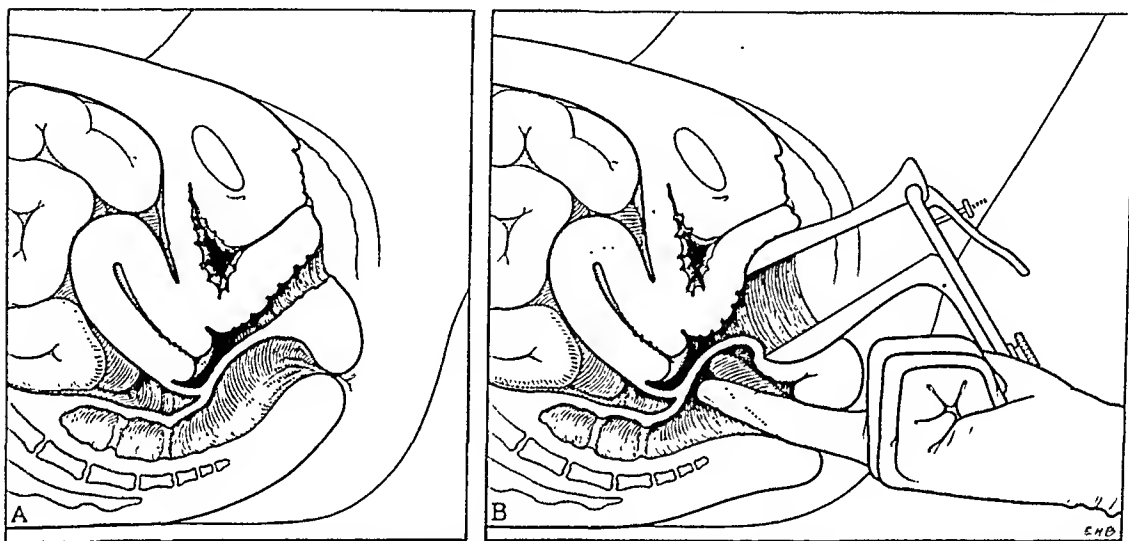


Fig. 1.—(A). Rectocele above firm perineal body. (B). Demonstrating rectocele. Withdrawal of speculum permits rectal wall to "fall away" from rectal finger, which follows into sacculated rectocele.

Since an enterocele must be recognized—usually *before* operation—to be eradicated *during* operation, not only must the awareness of its occurrence be cultivated, but also simple diagnostic steps taken to seek it out. It is rightfully regarded as a true hernia, for it is a saccular projection of the peritoneum of Douglas' cul-de-sac through a defect in the endopelvic fascia. This defect, either congenital or acquired, is between the uterosacral ligaments and opens the path for the peritoneal pouch protrusion into the areolar tissue between the enveloping fasciae of the rectum and the posterior vaginal wall. This herniation progresses until the structures of the inferior pelvic diaphragm (the perineal body) are encountered. It then may "roll over" these and present as a bulge at the introitus. In parous patients, the loss of anatomic semblance is confusing, for rectocele is a frequent complicating condition, and the co-existence of the two entities may be overlooked.

1. Nervous disorders, shocks, and frights. (A fairly large number of hypermenorrhea and menorrhagia were seen each year attributed to emotional upsets.) The necrotic end of an artery that has bled is apparently jarred loose by emotions such as fright or being upset nervously, initiating the bleeding.

### Summary and Conclusions

1. From 1935 to 1945, 5,210 women have consulted the gynecologic department of the University of Minnesota Student Health Service because of pain, vaginal discharge, and irregular uterine bleeding.

2. One thousand six hundred sixty-seven women, or 32 per cent, presented themselves because of irregular bleeding.

3. An accurate pelvic examination can be made with one finger bimanual and/or rectal examination.

4. Menorrheal irregularities are classified. Hormonal studies have been done on the urine in normal cases and on patients with cystic glandular hyperplasia, irregular shedding, and oligomenorrhea.

5. Opportunity to study the results of gonadotropic hormone administration can best be accomplished in an institution where the results can be better evaluated, and patient is saved the expense of hormone injections.

6. Abnormal uterine bleeding is frequently self-limited, and results due to spontaneous remissions or other fortuitous factors must be kept in mind before one judges the efficacy of any therapy.

7. X-ray therapy or radium have not been used in any of the students in this group.

8. Thyroid medication is probably still the best method of balancing the endocrine glands.

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these are not always conclusive. However, the simple combination of concomitant vaginal-speculum and rectal-digital examination is positively diagnostic. At the conclusion of the usual gynecologic examination of a patient presenting a "rectocele" either independently or in association with coexisting pelvic pathology, a bivalve speculum (Graves or other) is introduced deeply into the vagina with the posterior blade exposing the cervix and restraining the postvaginal wall. The index finger of the right hand is introduced into the rectum to the cervical level and maintained with palmar surface in contact with the anterior rectal (posterior vaginal) walls throughout the examination. The speculum is withdrawn first with the patient quiescent and then reintroduced and withdrawn while the patient strains or "bears down" forcibly.

The three drawings show the pelvic relationships found in the normal state, and with enterocele and rectocele. In the normal state, there is no rectal bulge into the vagina as a bivalve speculum is withdrawn. With either enterocele or rectocele, although the herniation is obvious, especially on straining, a differential diagnosis is not possible. If, however, a finger is carried high into the rectum and placed against the anterior rectal wall, and the patient is instructed to strain as the speculum is withdrawn, the existence of enterocele or rectocele or both is immediately determined and accurately diagnosed. If an enterocele is present, the bulge into the vagina begins below the cervix and progressively enlarges to its lower extent, while the anterior rectal wall is held in contact with the rectal finger. In rectocele, the bulge occurs lower in the vagina and, as the speculum is withdrawn, the anterior rectal wall "falls" away from the rectal finger, since the bulge is formed by the herniation of the anterior rectal wall into the vagina. If both enterocele and rectocele are present, the two observations are noted in sequence, with the rectal finger held in contact with the anterior rectal wall by the interposed enterocele, until the site of the perineal body is reached. Here the loss of fascial and muscle structure permits the forward herniation of the anterior rectal wall (rectocele) *beneath* the already diagnosed enterocele.

This technique can be used as the terminal diagnostic procedure in every patient presenting a posterior vaginal wall relaxation. In actual practice it consumes little time, but conclusively determines the exact status of the herniae encountered. It is definitive in the diagnosis of enterocele.

In proceeding to determine the nature of the protrusion of a posterior vaginal bulge, one must recall that an enterocele is dependent upon a fascial defect in the endopelvic fascia without necessarily any impairment in the enveloping fasciae of the vagina or rectum, whereas a rectocele is a hernia directly dependent for its development upon loss of the fascial support of the

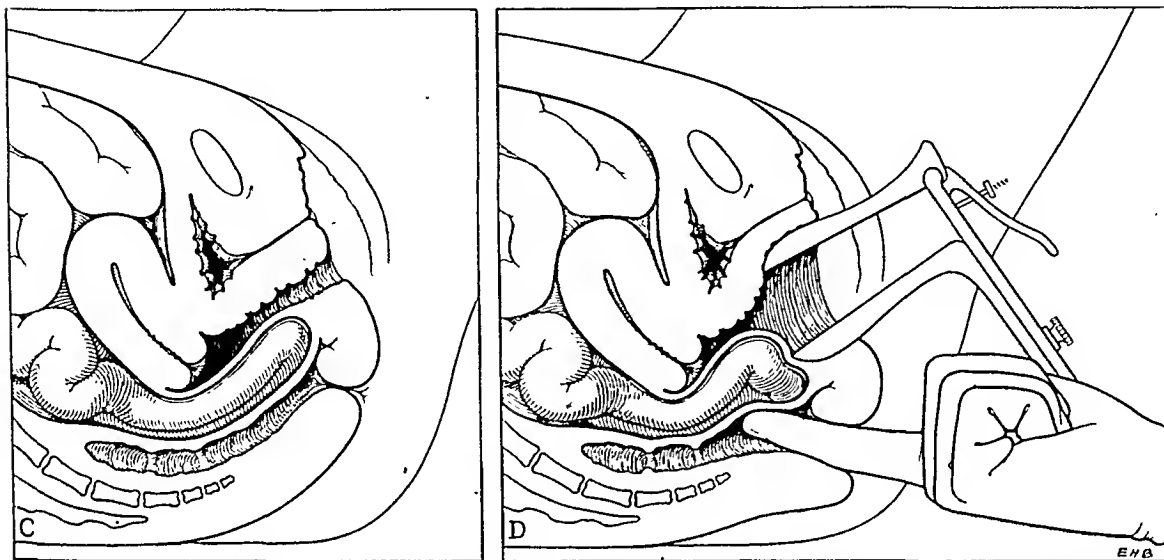


Fig. 2.—(C). Large enterocele without rectocele. (D). Demonstrating enterocele. On withdrawing the speculum the enterocele bulges into the vagina, but the rectal wall maintains contact with the rectal finger, for the enterocele separates and "fills" the rectovaginal septum.

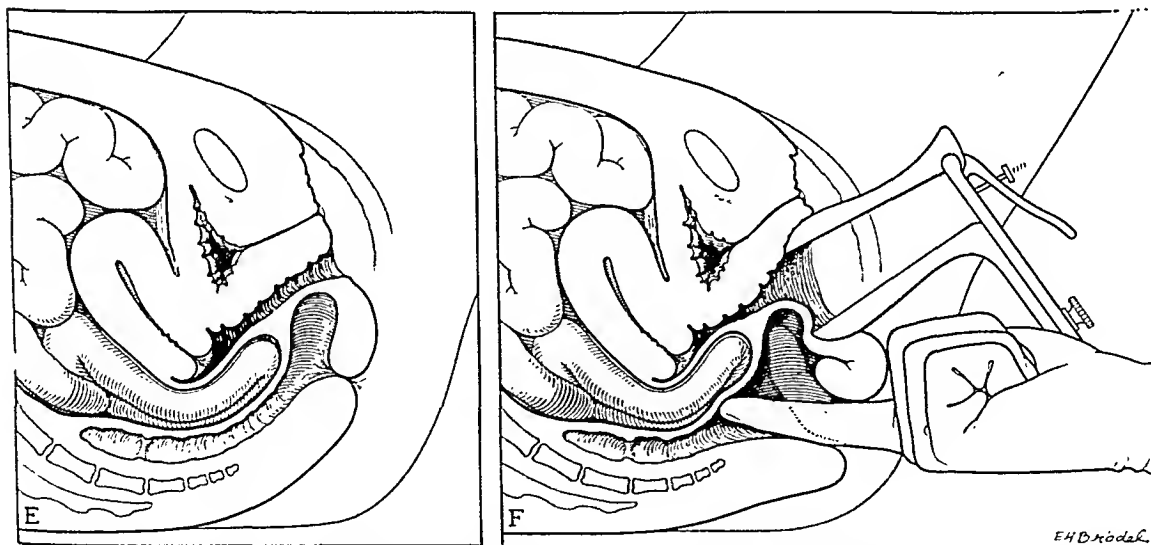


Fig. 3.—(E). Enterocele and rectocele. (F). Demonstrating enterocele and rectocele. As the speculum is withdrawn, the enterocele herniates into the vagina but the rectal wall maintains contact with the rectal finger, as in D. Further speculum withdrawal reaches the site of rectocele, and now the rectal wall falls forward away from the finger, which must flex to maintain contact, as in E.

posterior vaginal wall and rectum through injury of the fused levator and urogenital diaphragm fasciae. Since injury plays a large role in their evolution, the association is expected.

The common methods employed to diagnose enterocele are manual and speculum vaginal examination and rectal digital examination. In my opinion,



packages. Table I gives the indications (toxemia, placenta previa and abruptio placentae, disproportion and dystocia, previous cesarean section, or miscellaneous) for the cesarean section, and correlated with it is the type of anesthetic in relation to febrile and afebrile convalescence. Febrile means that the patient had a temperature of 38° C. (100.4° F. or more) on two or more days, excluding the first postpartum day. The four groups of anesthesia for this and the other table are local, local and gas, gas, and caudal. In 10 patients that had cesarean section in which sulfonamides were placed within the uterine cavity, seven were afebrile, while three were febrile. Eight of these 10 patients had local anesthesia, and two had local and gas. A second group is composed of 15 patients who had Porro cesarean section in 1942 to 1943 (during the same time that the former group was observed). Of this number, 12, or 80 per cent, were afebrile.

TABLE I. INTRAUTERINE SULFONAMIDES IN CESAREAN SECTIONS AND PORRO SECTIONS DURING THE PERIOD OF THE STUDY

	INTRAUTERINE SULFONAMIDES 10 LAPAROTOMIES		PORRO CESAREAN SECTIONS WITHOUT SULFONAMIDES	
	AFEBRILE 7	FEBRILE 3 (30%)	AFEBRILE 12	FEBRILE 3 (20%)
Toxemia	2	0	0	0
Placenta previa and abruptio	0	0	2	2
Disproportion and dystocia	3	2	1	0
Previous cesarean section	1	1	3	1
Miscellaneous	1	0	6	0
Local	6	2	0	0
Local and gas	1	1	2	2
Gas	0	0	8	1
Caudal	0	0	2	0

TABLE II. CESAREAN SECTIONS WITH AND WITHOUT SULFONAMIDES UNDER THE VESICO-UTERINE PERITONEUM

	SULFONAMIDES UNDER THE VESICO-UTERINE PERITONEUM		CONTROL GROUP OF 125 NO SULFONAMIDES	
	AFEBRILE 27 (63%)	FEBRILE 16 (37%)	AFEBRILE 90 (72%)	FEBRILE 35 (28%)
Toxemia	2	1 (33%)	11	6 (35%)
Placenta previa and abruptio	2	1 (33%)	14	8 (36%)
Disproportion and dystocia	8	10 (56%)	29	13 (31%)
Previous cesarean section	13	4 (23%)	25	5 (17%)
Miscellaneous	2	0 (0%)	11	3 (21%)
Local	6	10 (63%)	50	15 (23%)
Local and gas	6	3 (33%)	14	5 (26%)
Gas	6	1 (14%)	22	12 (35%)
Caudal	9	2 (18%)	4	3 (43%)

For a control (untreated) group (Table II) of cesarean section, 125 unselected or uncorrected patients were chosen. Ninety, or 72 per cent, were afebrile, whereas 35, or 28 per cent, were febrile. This percentage is more statistically significant since the total number is large. Nevertheless, 72 per cent does not differ greatly from the 80 per cent when it is realized that there were but 15 patients in the other series. Febrile courses occurred in all five clinical divisions of toxemia, placenta previa and abruptio, disproportion and dystocia, previous cesarean section, and miscellaneous groups. Likewise, febrile courses followed all types of anesthesia.

The treated group consisted of 43 patients. The incision in the uterus was closed in the routine fashion. When the area covered by the detached

## SULFONAMIDES AS A PROPHYLACTIC AGENT IN CONJUNCTION WITH CESAREAN SECTION

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AFTER the therapeutic value of sulfonamides was established, it was proposed that one or more of them might be used in a prophylactic fashion. Various reports have been given. The Army and Navy Medical Corps gave trials on prophylactic value for injuries sustained in combat and for venereal exposures. The purpose of this presentation is to give our observation on the deposition of sulfanilamide in forty patients and sulfathiazole in three patients under the peritoneal reflection from the urinary bladder to the uterus in association with the closures of the uterine wound at the time of cesarean section.

### Techniques

Obviously, any reduction in puerperal febrile morbidity is most desirable. If the infection occurred along the incision or in traumatized tissue, then it might be prevented by the use of sulfonamides in these sites. Without any particular guide, a little exploration was attempted. At first, sulfonamides were placed in the uterine cavity with the routine intrauterine small pack. This pack was removed vaginally in eight hours. Not enough was absorbed to yield even a trace in the blood tests. Clotting occurred about the crystals, which likely made a complete barrier to absorption.

To confirm these first findings, sulfonamide powder was encased in a thin cloth sack and it was placed in the uterine cavity with the pack. A blood clot formed around the pack also. As nearly as could be determined, none of the sulfonamide had been removed. Since this exploration exposed the inadequacy of the free intrauterine application for prophylactic use, a direct application of sulfonamides to the incised uterine wall seemed appropriate for investigation.

Practically all of the cesarean sections at the Chicago Lying-in Hospital are performed by the laparotrachelotomy technique. This technique entails the detachment of the vesico-uterine peritoneum at its attachment to the uterus (just below the "white line") and the reflection downward of this peritoneal layer which then exposes the lower uterine segment. A sagittal incision is made through the lower segment wall in this exposed area, but occasionally the incision is extended upward beyond the "white line." The uterine wall incision is closed in two layers. The first by interrupted catgut suture and the second layer including the fascia by a continuous catgut stitch. The vesico-uterine peritoneum is reattached back to the uterus to its original site or above, if necessary, to cover completely the incision. Accordingly, this space, formerly composed of loose areolar tissue, was an area in which deposition of sulfonamide powder might have some value in preventing infection in the uterine incision or adjacent tissues, and yet not interfere with wound healing of uterine wall. It has been observed that direct spread of endometritis may pass rapidly through the incision.

### Results

Sulfathiazole was employed in only a few instances, while sulfanilamide was used generally because it was available in commercially prepared sterile

### Conclusions

From these observations, it is evident that the use of sulfonamide locally did not lower the morbidity rate nor shorten convalescence. Furthermore, the bladder peritoneum seemed more adherent in a few patients subjected to laparotomy subsequently. This may not be serious, but it requires greater caution in the reflection of this tissue in subsequent laparotrachelotomies.

Therefore, the local deposition of sulfonamides, either within the uterine cavity or over the uterine incision (but under the peritoneal reflection) did not reveal any prophylactic value. It did increase adhesions of the peritoneum to the uterus. There exists also the dangers of drug sensitization.

The sulfonamides in relation to cesarean section should be used on direct indication in relation to a proper bacteriologic study of the uterine cavity and blood stream, except in such urgent situations where the withholding of the drug would jeopardize the patient's convalescence or life. Even in this event today penicillin would seem preferable to the sulfonamides with but few exceptions. Penicillin, like any other medicament, should be employed in sufficient and proper dosage and only when properly indicated.

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vesico-uterine peritoneum was free from blood and dry, 5 Gm. of sulfonamide powder was deposited over the uterine fascia. The peritoneum was reattached to the uterine wall, covering the sulfonamide powder. Special efforts were made to keep the sulfonamide within this zone and out of the free peritoneal cavity. In this group of 43 patients, 16 of them, or 37 per cent, were febrile. This is the highest febrile group in the entire series, in spite of the fact that an effort was under way to reduce or prevent a febrile course. Moreover, there was no evidence that the febrile reaction in any of these was on a basis of drug sensitization.

The cesarean sections were performed electively in several instances because of a previous cesarean section. It will be noted that the disproportion and dystocia group had 10 febrile to the eight afebrile. In the control group, local anesthesia was used more than all others, while in this limited series local anesthetics alone were not so dominant.

Richards<sup>1</sup> believes that local implantation should be beneficial, but his number of patients are too small to be conclusive. Anderson and associates<sup>2</sup> demonstrated that an intrauterine pack completely filling the uterus can be left in situ for a protracted period when the sulfonamides are impregnated or placed in the pack. We observed one patient who had a pack in the uterus for twelve days without febrile reaction. Because of a blood dyscrasia the pack was left for this time. Sulfathiazole was added to the pack and penicillin given hypodermically over this entire period. The small pack customarily employed in laparotomies could not compare to the tight pack for postpartum hemorrhage. Ramos<sup>3</sup> advances great claims for the use of sulfonamide therapy in a prophylactic manner at the time of cesarean section. Their number of untreated patients was 429, with a mortality of 4.89 per cent. There were 69 patients which they treated, with a mortality of 1.45 per cent. He did not discuss other therapies, as blood transfusion and improved techniques. The mortality rate of 4 per cent is entirely too high by the standards of the better maternities in the United States. Perhaps Ramos is dealing with a different type of patient than that which is encountered in the Chicago Lying-in Hospital.

### Blood Levels

Hesseltine<sup>4</sup> reported blood levels on 32 patients (30 who had 5 Gm. sulfanilamide, and two who had 5 Gm. sulfathiazole). Readings were made at the fourth, eighth, twelfth, and twenty-fourth hours after the deposition. One test was made at the sixteenth and also twentieth hours.

The ranges for the two patients on sulfathiazole are:

Hr.	4th	8th	24th
Mg.	3.0	2.6	1.9
Mg.	1.0	--	--

The thirty on sulfanilamide had ranges at fourth, eighth, twelfth, and twenty-fourth hours as follows:

Hr.	4th	8th	12th	24th
Highest	10.8	10.0	6.9	6.7
Lowest	1.0	1.8	2.0	1.5

The average of the sulfonamide levels are:

Hr.	4th	8th	12th	24th
	3.3	4.0	3.8	3.0

This indicates that good absorption can be expected from this site. However, rates are so erratic and unpredictable that this is an unsatisfactory channel for establishing effective and dependable levels.

had manifested slight albuminuria, but, according to her doctor's report, this had cleared up in a short time. The course of pregnancy was then uneventful until one month before admission when there was a return of albuminuria and, for the first time, hypertension was observed (140/90). There was a weight gain of 28 pounds during the entire course of pregnancy. When hospitalization was advised because of the signs of toxemia, the patient refused, and during the ensuing four weeks hypertension continued, accompanied by headaches and pedal edema. On the day prior to admission, the patient exhibited restlessness and epigastric pain, followed by a generalized convulsion on the morning of admission. The convulsion lasted ten minutes, followed by unconsciousness; she was then admitted to the hospital.

Review of the past history was void for scarlet fever, nephritis, pyelitis, hypertension, or contagious diseases. Menses began at 18 years of age and were accompanied by severe occipital headaches throughout her adult life. Both the patient and her robust brother give a history of fainting upon slight provocation, especially with emotional excitement. There was vomiting during the first trimester, with return of that symptom two weeks prior to admission.

On admission, the patient was observed to be obviously in the third trimester of pregnancy, having generalized tonic and clonic convulsions (apparently the second seizure). Her temperature was 98.6° F., pulse 145, respiration 30, and blood pressure 207/160. Examination of the eye grounds revealed bilateral peripapillary edema, numerous points of A-V notching, without great disproportion in the A/V ratio. One flame-shaped hemorrhage was noted. Examination of the chest revealed gallop cardiac rhythm and moist pulmonary rales at both lung bases. Edema of the extremities was described as slight. Other than the obstetric findings (eight to eight and one-half months pregnancy, not in labor, vertex presentation, normal fetal heart tones) the remainder of the physical examination was negative.

The following laboratory data were obtained on admission: *Urine*: albumin 65 per cent moist (Purdy); sugar: negative; sediment: 10 red blood cells, 20 white blood cells, few hyaline casts (high power field). *Blood Chemistry*: carbon dioxide, 22; urea, 16.7; glucose, 87. *Venous Pressure*: 175 mm. H<sub>2</sub>O.

Eclampsia was handled by the usual methods of dehydration and sedation. No further convulsions were experienced. Onset of labor was spontaneous, and delivery was accomplished by low forceps and episiotomy under local analgesia the following afternoon. Blood loss at delivery was estimated at 400 c.c. Blood pressure prior to delivery was 150/100, but by the conclusion of the delivery it had fallen to 78/50, although delivery was accomplished without difficulty and the third stage was entirely normal. Shock was treated by transfusions of citrated blood and pooled plasma, without effect on the blood pressure. Two doses of adrenalin intravenously were required to elevate the blood pressure above shock level, after which it became stabilized at 90 to 100 systolic. It was estimated that the blood pressure remained at severe shock level for about one and one-half hours and at mild shock level for about nine hours, during which time 4 c.c. of Eschatin were given intravenously. The pulse rate remained at 132 for eighteen hours. Because of very poor urinary output during the first twenty-four hours after delivery, diathermy was given over the kidney areas and hypertonic glucose was administered in large quantities, intravenously, with Ringer's lactate solution to combat the acidosis. Improvement was slow, but by the fourth hospital day, the urinary output had reached 700 c.c. for a twelve-hour period.

Because of a marked anemia, on the seventh hospital day the patient was given a transfusion of 500 c.c. of citrated blood. By error this was followed by a liter of distilled water. Before the error was detected, the entire infusion had drained and the patient complained of generalized aching, had several

## ACUTE POSTPARTUM NECROSIS OF THE ANTERIOR HYPOPHYSIS

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WE HAVE recently (publication of case delayed by military service) had experience with a case of acute postpartum necrosis of the anterior hypophysis, wherein the patient exhibited spontaneous hypoglycemia of a severe degree and survived the acute episode long enough to display some of the manifestations of Simmonds' disease. Because of the infrequency of cases wherein the clinical diagnosis has been made, followed by a temporary recovery, subsequent death, and autopsy, we desire to report this case in some detail.

Much confusion is apparent in the present-day literature regarding the physiology of the anterior pituitary, but some light is being brought into the picture by the increasing attention to destructive lesions of the anterior lobe, following shock at delivery, resulting in the clinical picture of Simmonds' disease. In 1883, Simpson<sup>1</sup> described the syndrome, described the clinical course, and mentioned etiologic factors, but it was not until 1914 that Simmonds<sup>2</sup> described the pathology of the disease that bears his name. Maresch,<sup>3</sup> in the same year, called attention to the fact that hypopituitarism was likely to occur in patients who experienced repeated labors, especially when accompanied by hemorrhage. He maintained that those cases represented functional exhaustion of the pituitary gland. Silver,<sup>4</sup> in 1933, reported that in 26 out of 39 autopsies on cases of Simmonds' disease there was atrophy or fibrosis of the anterior pituitary. He explained the etiology of this pathologic picture by assuming embolism of the pituitary vessels, as a result of puerperal sepsis.

The recent work of Sheehan<sup>5-8</sup> and Murdoch has shown conclusively the close relationship between postpartum necrosis and shock and hemorrhage at delivery. Since the work of these investigators, isolated reports have appeared in the literature. In 1942, Escamilla<sup>9</sup> and Lissner presented the most complete review and analysis of the literature to date. They collected data on 595 cases suggestive of Simmonds' disease in one form or another. This valuable material was gathered from a thorough search of the literature, personal communications, and their own cases. All cases were subjected to critical analysis regarding etiology, symptomatology, and treatment. According to their study, there had been until that date 27 cases of Simmonds' disease, upon which autopsies had been performed, and the etiology established as originating from massive necrosis of the anterior hypophysis, accompanying collapse or hemorrhage at delivery.

### Case Report

Mrs. L. V., a 32-year-old white primigravida, was admitted to the Charity Hospital on April 11, 1942, having generalized convulsions. The last normal menstrual period had been on July 4, 1941, and the patient had been under a physician's care since the sixth week of pregnancy. At the third month she

On the fifteenth hospital day, the patient was able to sit up in a chair all day, and visit her baby in the nursery. Blood chemistry on this day: urea, 59; creatinine, 5.5; glucose, 58; chlorides, 445. Two days later, the patient developed signs of a thrombophlebitis (secondary to glucose administrations) in the right saphenous vein. The following day the saphenous and femoral veins on that side were ligated, followed by lumbar sympathetic block. During the next few days the patient ran a septic course and the general condition became worse. Urinary output diminished, and pyuria became marked.



Fig. 1.—Enlarged photograph of sectioned pituitary gland, showing massive necrosis of anterior lobe.

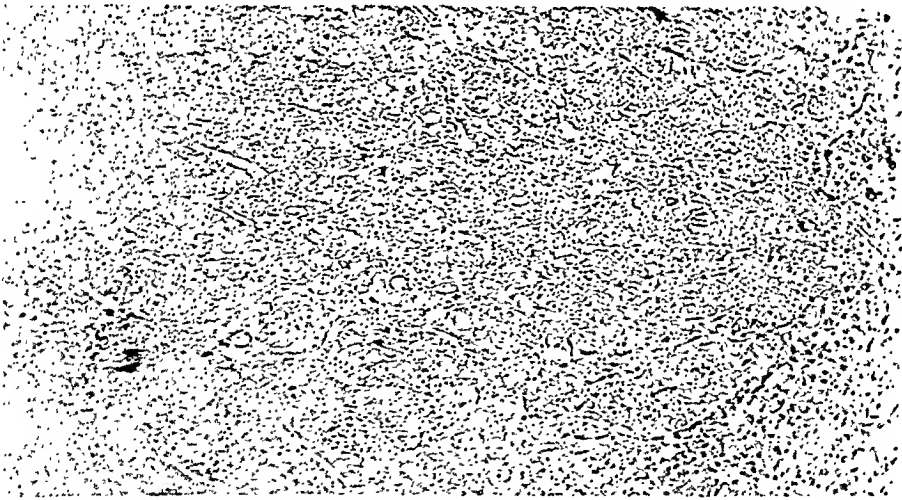


Fig. 2.—Photomicrograph of necrotic area of anterior pituitary, showing a few glandular elements at periphery.

With general supportive therapy, the condition again improved, and on May 3 (22nd hospital day) thyroid therapy was started. Two days later the patient relapsed and again the septic picture became pronounced. On May 7, generalized maculopapular spots appeared, and blood culture was reported as positive for *Staphylococcus albus*. Blood chemistry: urea, 108; creatinine, 10.5; sugar, 266; chlorides, 515 (infusions had been discontinued, fluid intake was very poor, and this was interpreted as being very concentrated). Repeated blood cultures continued positive for *Staph. albus*, and, despite heroic measures, the patient died on May 11.

Autopsy performed immediately following death revealed the following: Pituitary: weight: 0.506 Gm. In the anterior lobe there was a yellow depressed

loose stools, and became stuporous. The blood pressure rose to 180/110, the rectal temperature dropped to 95° F., and mucus accumulated in the throat. Twelve hours later the patient was in a moribund condition. Because of acidosis, and the clinical impression of hypoglycemia, 300 c.c. of 5 per cent soda bicarbonate followed by 50 c.c. of 50 per cent glucose was administered intravenously. Within thirty minutes there was a dramatic change in the patient's condition. She was relieved of coma, appeared alert, responded to questions, and was able to supply missing details in her past history. An infusion of 1,000 c.c. of 10 per cent glucose was then given. It was noted here (as it had been on the day after admission), that despite administration of large quantities of glucose intravenously, *no glucose spilled over into the urine nor was there any appreciable rise in the blood sugar*. That evening the patient again required administration of 50 per cent glucose intravenously to combat a relapse into a semicomatose state. Again, the response was dramatic. Blood chemistry taken after response showed: nonprotein nitrogen, 30; glucose, 104; carbon dioxide, 48.

The following morning the blood chemistry showed: urea, 61; glucose, 62; carbon dioxide, 44; serum proteins, 5.11. A continuous drip of hypertonic glucose was given throughout the day, and administration of adrenalin min. V raised the blood pressure to 190/90, but failed to produce a rise in the blood sugar level, or promote glycosuria, despite the infusion.

On the ninth day, despite continuous administration of 20 per cent glucose by intravenous drip, the patient became comatose, requiring 50 per cent glucose to relieve the coma. It was then decided that in all probability the case was one of pituitary necrosis, so whole antuitrin therapy was begun. No effect was observed after twelve hours, during which time 11 c.c. was administered, so this therapy was abandoned.

The following day, desoxycorticosterone acetate therapy, in conjunction with regulated sodium chloride administration, was started. Twenty mg. of DOCA was given in the first twenty-four hours, with a maintenance dose of 15 mg. day thereafter. One liter of normal saline was allowed per twenty-four hours. At this time, the nonprotein nitrogen was 75; urea, 52; creatinine, 9.7; glucose, 64; plasma chlorides, 445; carbon dioxide combining power, 44. Another transfusion was given, without incident, and improvement seemed to follow. The urea nitrogen fell to 48, and the glucose rose to 85. The patient remained rational, and apparently the DOCA was achieving its purpose, because 50 per cent glucose was no longer required, although hypertonic glucose infusions were continued for a few days.

It was noted that lactation had never occurred and that the breasts were very small. Urinary output at this time was excellent. On the thirteenth day the patient's condition was good, and infusions were discontinued. Blood Chemistry: urea, 50; creatinine, 7; glucose, 64; chlorides, 574. It was noted here that, although there was not much apparent improvement in the blood chemistry findings, still, definite improvement was reflected because these were interpreted as true values, whereas previous specimens were considered to have been greatly diluted, because of the continuous infusions.

When it was attempted to reduce the dose of DOCA, within twenty-four hours the patient relapsed into a comatose state, with mild convulsions. Blood glucose was reported as 48. Rectal temperature was 95° F. With administration of glucose and increased dosage of DOCA (5 mg. every six hours, rather than every twelve hours) the patient's condition again rapidly improved.

The basal metabolism rate was determined and found to be -31. It was noticed that brownish pigmentation, previously noted, seemed to be increasing, especially over the arms. X-ray of the chest revealed no disturbance of the cardiothoracic ratio.



delivery. It has been suggested that there is thrombosis of the pituitary vessels, but this has never been shown consistently at autopsy. More likely, associated with general collapse, there is collapse of the vessels and sinusoids in the gland itself. If prolonged, this could, in itself, produce the typical picture of ischemic necrosis. However, stagnation and physiochemical changes in the blood might conceivably account for the small thromboses seen in the smaller vessels, within the gland substance, and the theory of thrombosis seems to hold. In any event, microscopic examination of the necrotic area always gives the typical appearance of ischemic necrosis—infarction. Various authors (Silver, Rieker, Curtiss) emphasize the importance of puerperal sepsis, and attribute the necrosis to embolic phenomena. It is the opinion of most authors, however, that sepsis plays a minor role in most cases.

### Treatment

The results of treatment, to date, have been so discouraging that prophylaxis bears more emphasis. Improved obstetrics, proper prenatal supervision, careful conduct of the third stage, and the judicious management of the complications of pregnancy, especially those which predispose to hemorrhage and collapse, are of utmost importance. Preliminary blood matching and "Rh" determination of "dangerous cases," vigilant observation for the early signs of shock, and the prompt, or better, prophylactic administration of blood and/or plasma assume an even greater obstetric significance in the light of pituitary necrosis. Sheehan has shown that 25 per cent of patients suffering collapse at delivery subsequently exhibit evidence of Simmonds' disease.

Second in importance to prophylaxis is early diagnosis. This often must depend upon suspicion, or realization of the fact that conditions are present for the development of this complication. Treatment of the developed condition may be considered under two headings: early, and late. Early treatment is directed toward relieving shock, replacing blood loss, and correction of the obstetric situation which precipitated shock. The blood chemistry should be studied early and frequently. Hypoglycemia should be prevented, as many of these cases die in coma, undoubtedly associated with a hypoglycemic state. Secondary collapse or hemorrhage must be prevented, once the acute episode is controlled.

Unfortunately, most of the discussions of treatment in the literature are concerned with the therapy of Simmonds' disease, or the late effects of the necrosis, and little is offered in the management of the acutely developed condition. It has been shown in animal study that total hypophysectomy need not be followed by death. We have been able to locate only one article relating a human case report, and in this instance the gland had slowly lost its function by the development of a tumor. This patient was alive three years after total hypophysectomy, but demonstrated osteogenic effects and fairly constant hypoglycemia. We know of no instance where a patient survived the extirpation of an entirely normal pituitary gland. It seems likely, however, that such would be possible, because, in many of the cases of severe Simmonds' disease, postmortem examination years later has shown almost

area replacing about 85 per cent of the gland substance. Microscopically, practically the entire anterior lobe stained pink, without any cellular details. Only a few pyknotic remnants of nuclei were noted. Adjacent to the pars intermedia, a few acini were noted. The blood vessels showed thrombosis and occlusion. The posterior lobe was normal (Figs. 1 and 2). *Breast*: the acini and ducts were small and greatly separated by a large amount of adipose tissue. *Ovaries*: no Graafian follicles or corpora lutea were noted. *Uterus*: no endometrium was noted. *Adrenals*: grossly normal. Microscopically, the cells of the reticular and fascicular layers were highly vacuolated. The medullary cells stained darker than usual. *Lungs*: on the right there was a subpleural abscess, with apical pulmonary fibrosis. *Pancreas*: the pancreas weighed 100 Gm., and showed no gross or microscopic pathology other than an increased amount of loose fibrous tissue surrounding acini, ducts, and islets. *Kidneys*: right 100 Gm., left 135 Gm. The right kidney lay in the midline, adjacent to L4. It had a bizarre shape, and presented no definite hilum. Vessels entered at the superior pole. Ureter left the kidney from three sites. Capsules of both kidneys stripped with difficulty. There was indistinct demarcation between the cortex and medulla. Calices and pelvis of the left kidney were normal. The right renal artery and vein arose just above the bifurcation of the aorta and inferior vena cava, respectively. Microscopically, there was dilatation of the tubules and Bowman's spaces. In the interstitial tissues there were collections of polys and macrophages. *Right Femoral Vein*: firm gray blood clot 3 cm. long, extending into the external iliac vein.

### Discussion

The patient in whom postpartum necrosis of the anterior pituitary occurred may die early in the puerperium, either as a result of obstetric shock, or of the necrosis per se. In this instance, localizing symptoms and signs are difficult to define, and diagnosis may rest upon empiricism, if death occurs before fourteen hours have elapsed, examination of the pituitary will fail to reveal the lesion.

On the other hand, if the patient survives the immediate crisis, the clinical picture is distinct, although variable, and dependent upon the proportion of gland substance destroyed. Sheehan emphasizes the quantitative aspect of Simmonds' disease. It has been shown that patients may exhibit no symptoms following destruction of 50 per cent of the anterior lobe, while destruction of 75 per cent will give rise to moderate symptoms, and only with destruction of 90 per cent of the gland substance will severe clinical symptoms be given.

In the early puerperium, the only localizing signs are the inhibition of lactation, and occasionally hypoglycemia, later a characteristic pattern of signs and symptoms appear, depending upon the degree of pituitary damage. Amenorrhea, hypometabolism, hypoglycemia, hypopiasia, anemia, loss of body hair, apathy, asthenia, progeria, and occasionally, but terminally, cachexia are noteworthy manifestations of this condition.

The exact mechanism whereby pituitary necrosis is produced is unknown. Several factors conducive to the development of this strange phenomenon have long been known: (1) Hyperplasia of the pituitary during pregnancy; (2) the rigid bony cage enclosing the gland, resisting the hypertrophy; (3) sinusoidal arrangement of the blood vessels in the parenchyma. Incongruously we must admit the very rich blood supply afforded by the circle of Willis. The initiating mechanism, at any rate, begins with collapse from shock or hemorrhage at

prepared still retains the major portion of the total activity of the crude extract. The chemically impure amorphous substance remaining in the mother liquor has been shown to be capable of maintaining life in the adrenalectomized dog in  $\frac{1}{15}$  of the amount required of DOC and  $\frac{1}{100}$  the amount required by corticosterone.<sup>13</sup>

For gluconeogenesis, corticosterone, compound E, and their derivatives with oxygen on C11 are necessary, whereas DOC appears to have the most marked effect on the distribution of electrolytes. For the maintenance of normal adrenal function, the amorphous fraction is most efficient.<sup>14</sup> It has been stated<sup>11</sup> that carbohydrate metabolism is somewhat dependent upon electrolyte and water balance, as shown by the fact that adrenalectomized animals can be maintained with regards to blood sugar and liver glycogen, on a diet high in salt and water, even in the absence of adrenal cortical hormone. However, these animals are peculiarly susceptible to stress, and even mild stimuli may precipitate against insulin in the insulin-sensitive adrenalectomized animal.<sup>11</sup> It has been shown that adrenalectomized animals have lowered resistance to toxins and infections. There is an appreciable decrease in antibody formation, and the whole defensive mechanism seems to be less responsive after adrenalectomy.

Hartman reported a lactation factor,<sup>15</sup> which enabled female rats to lactate in the presence of adrenal insufficiency. Compound E is also said to be effective in promoting lactation.

In planning cortical replacement therapy, one is confronted with the problem of substituting control of two widely different functions of the adrenal cortex, namely the maintenance of normal water and electrolyte balance, and the regulation of carbohydrate metabolism. The changes relative to disturbed water and electrolyte metabolism may be relieved by DOC; those related to carbohydrate metabolism may be remedied by whole cortical extract, or the corticosterone series, compounds A, B, E, and F of Kendall.

4. *Anterior Pituitary-like Hormones*.—Some success has been reported with the use of progesterone. This is easily understood, in the light of the above.

5. *Thyroid*.—While Sheehan<sup>7</sup> has contended that the use of thyroid extracts may be dangerous, he reports good results in the myxedematous type of patients. On the other hand, J. H. Means<sup>16</sup> has shown that it is exactly this type of patient that presents the real danger in employing thyroid therapy. The complication most to be feared is the development of sudden adrenal cortical failure. To prevent this, Means recommends high salt intake and anterior lobe extracts. He reports two cases of pituitary failure, associated with myxedema, treated by thyroid extract. The first patient died, showing true Simmonds's disease with diffuse fibrosis of the anterior pituitary. The other patient was rescued by salt therapy. The patient we have presented was apparently made worse by thyroid therapy.

6. *Pregnancy*.—Sheehan<sup>7</sup> has suggested that the most promising hope in a case of Simmonds' disease resulting from pituitary necrosis is the occurrence of another pregnancy. It appears that in nearly every instance where another pregnancy ensued, there was clinical cure, or marked remission of the symp-

complete destruction of the anterior hypophysis. Be that as it may, extensive necrosis is a major shock to the normal physiology, and some sort of substitution therapy should be attempted.

1. *Pituitary Extracts*.—There are reports of success following the use of various extracts of whole anterior pituitary substance. This line of therapy is entirely rational, but, unfortunately, feeble. The available extracts are of uncertain potency, as there is no chemical or biologic standardization. The only thing certain is their impotence, and it may be stated that they fall in the general category of "endocrine soups." In the future, with improved chemical methods, much is to be expected from this line of therapy, but for the present we must rely largely upon other therapeutic weapons.

2. *Glucose*.—Glucose is invaluable in those cases exhibiting disturbed carbohydrate metabolism, but it must be remembered that tolerance to glucose will increase until functional exhaustion of the islets of the pancreas occurs. Then diabetic failure will supervene. Nevertheless, concentrated glucose should be employed generously until carbohydrate metabolism can be regulated. As well shown by this case, one must be more than attentive to the veins of patients receiving hypertonic glucose, because, while the glucose may be life-saving, the administration may indirectly cause the death of the patient as a result of phlebitis and septicemia.

3. *Adrenal Extracts*.—Because of the rather acute adrenal failure secondary to removal of pituitary stimulation, attention must be given to replacement therapy until such time as pituitary function can be restored or replaced. While pathologic changes in the adrenals have been consistently reported, there is no reason to assume primary adrenal damage, so that replacement therapy is dependent upon absence of pituitary stimulation.

There are no hard and fast rules governing the dosages of adrenal extracts in the acute crisis. Empiricism must be practiced at first and, after balance has been established, the general rules applied in most cases of Addison's disease may be followed, depending upon the severity of the case. It must be remembered, however, that just as in Addison's disease, potassium restriction is just as necessary as sodium administration.

In the treatment of acute cortical deficiency, most authors agree that the administration of whole cortical extract is preferable to the use of desoxycorticosterone acetate. Kendall<sup>10</sup> has listed eleven steroids of known formulae, in the corticosterone group. In addition to these, the adrenal cortex is known to contain desoxycorticosterone, progesterone, estrone, and certain androgens.<sup>11</sup> Of special significance are the steroids designated by Kendall as Compounds A, B, E, and F. These four steroids all contain an oxygen atom on C11, which desoxycorticosterone does not, and this is of importance in carbohydrate metabolism. Kendall<sup>12</sup> credits the ketol structure on C17 for enabling the cortical hormones to maintain life in the adrenalectomized animal. Progesterone possesses such a group, and has been shown to be capable of prolonging life in the adrenalectomized animal.<sup>11</sup>

It is interesting to note that, despite the isolation of so many chemically pure steroids from the adrenal cortex, the mother liquor from which they are

## PROLAPSE OF THE UMBILICAL CORD

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OUR attention was drawn to the study of this unfortunate accident of labor because of an unusual grouping of cases which followed one another with alarming rapidity, and because of dissatisfaction with the results of our treatment. Survey of the literature did not help us to define the problem and formulate its solution, for we encountered frequent acceptance of types of treatment which were obviously unsuccessful and at times outmoded by recent obstetric advances. We were therefore led to a study of 71 cases of prolapsed cord which had occurred in our hospital during the period of ten years prior to this analysis. Our incidence approximated the 0.42 per cent reported by Bourgeois<sup>6</sup> in 1941.

*Etiology.*—In seeking etiologic factors we studied parity, presentation, and pelvic type with the following findings:

1. *Parity:* There were 29 primiparas in our group. This does not allow any conclusions regarding the significance of parity as an etiologic factor in our cases. Mengert and Longwell<sup>5</sup> have stressed the dangers of operative delivery in this group, for they found the fetal mortality in primigravidas almost twice that of multiparas. This is a significant consideration.

2. *Presentation:* We have encountered a similar preponderance of abnormal presentations to that reported by others.<sup>1-4</sup> Our series includes:

Vertex	30
Breech	20
Transverse	7
Compound	1
Twins	13—of these twins:

Vertex	14
Breech	9
Transverse	2
Compound	1

This incidence is understandable, for the presentation other than vertex makes the cord more likely to prolapse through the unfilled lower uterine segment.

3. *Pelvis:* We have not found a high percentage of contracted pelvis. In our group of 71 cases, the pelvis were classified (clinically for the most part) as follows:

Gynecoid	51
Android	8
Anthropoid	9
Flat	3

In the entire group 65 were considered adequate for labor; six were considered small. This does not indicate that bony dystocia was an important element. It is in accord with the observations of Bourgeois, who believed other manipulative or accidental factors to be more important etiologically. He stressed the dangers in this regard of bagging or manual rotation of high heads, and also such accidents as premature rupture of the membranes and increased

toms, beginning in the early weeks. However, one of his cases experienced the almost unbelievable complication of another, a second pituitary necrosis in the subsequent pregnancy, and this was clearly demonstrated at autopsy. The physiologic hyperplasia of the pituitary during pregnancy, is, of course, the underlying basis for the improvement in his cases, and this leads to two interesting speculations. First, how is one to enhance the chances of pregnancy in a woman with Simmonds' disease, when the possibilities are so very poor, by the very nature of the disease? Second, what is the cause of the physiologic hyperplasia of the pituitary in pregnancy? While the latter might seem a very elementary question, because of its very simplicity it seems to have eluded solution. When the answer to this second question is known, the problem of replacement therapy may be approached on a much more rational basis.

We wish to express our appreciation to the Department of Pathology, Charity Hospital, for their assistance in studying this case, particularly Dr. Emma Moss, who made valuable suggestions regarding clinical studies, and Dr. Philip Pizzolato, who performed the autopsy.

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TABLE III. INCOMPLETE CERVICAL DILATATION—LIVE BABIES

CASE NUMBER	TREATMENT
6	Cord replaced; bagging; version and extraction
10	Full dilatation allowed; version and extraction
42	Manual dilatation; version and extraction
60	Full dilatation allowed; spontaneous breech delivery
62	Attempt at replacement and bagging; cesarean section
69	Cesarean section
70	Dührssen's incision; breech extraction

In breaking down the other group of failures, the instances of incomplete cervical dilatation where the infants did not survive, one first encounters eight of these 19 cases where the infant was either nonviable or in such poor condition before treatment was attempted that survival was unlikely. For the rest, attempts at cord replacement, Braxton-Hicks version, or expectant treatment were all attended by a notable lack of success. Furthermore, this group harbored the two maternal deaths in the series: No. 31 died of cervical laceration, hemorrhage, and shock initiated by attempts at manual dilatation of the cervix and breech extraction—moreover, this operation was attempted in the face of known intrapartum death of the child; No. 49 died of peritonitis resulting from rupture of a lymphogranulomatous rectal stricture—this was incurred during bagging and later breech extraction of a dead fetus.

### Conclusions and Recommendations

1. As in other serious disorders where treatment is difficult, early recognition is most important. We therefore advise: (a) prompt pelvic examination when the fetal heart indicates fetal distress; (b) scrupulous attention to the time of rupture of the membranes in breech and transverse presentations and multiple pregnancies; immediate pelvic examination unless contraindicated.

2. Successful outcome is to be anticipated with full cervical dilatation by the use of the appropriate obstetric operation: forceps delivery, breech extraction, or version and extraction, carried out promptly but without undue haste. It is wise to allow fetal recovery from anoxia (after elevation of presenting part) before attempting delivery.

3. Improvement in results with incomplete cervical dilatation might be obtained by pursuing the following policy: (a) with recognition of a prolapsed cord, the patient should be transferred to a delivery room table, placed in combination lithotomy Trendelenburg position, anesthetized with oxygen-ether by a trained anesthetist, and examined under sterile conditions. (b) the examiner should lift the presenting part out of the inlet in an effort to relieve pressure on the cord. (c) if the fetal heart returns to normal and if the patient is primiparous, or the cervix less than 3½ dilated, the patient should be subjected to cesarean section. While preparations for operation and induction of full anesthesia are completed, the examiner should continue to hold the presenting part out of the pelvis; the fetal heart should be checked repeatedly. (d) If the patient is multiparous and the cervix is 3 or more fingerbreadths dilated, it may be possible to secure safe operative dilatation by the use of the dilating bag. This of course calls for prior replacement of the cord which will be possible only with lesser degrees of cord prolapse.

pressure incidental to struggling under anesthesia. Mengert and Longwell were of the opinion that premature rupture of the membranes was less important than length of cord.

It is evident in general that many factors, whose incidence and onset are uncontrollable, play an important etiologic role in prolapse of the umbilical cord. Therefore, early recognition and prompt efficient treatment are necessary to meet this problem. It is of interest to point out here that there were seven cases of *cord presentation* during this same ten-year period of study and to note that there were no fetal deaths in this group. Of these seven cases, three were discovered on the delivery table when the cervix was fully dilated and the patient ready for delivery, while four were discovered during a pelvic examination which was performed for failure to progress, irregularity of fetal heart, or unduly high station of the fetal head.

*Fetal Survival.*—Fetal salvage was poor. In our group was noted:

Total babies who died	28 (39 per cent)
Viable babies who died	23 (32 per cent)

Breakdown of this fetal mortality reveals the major significance of the degree of cervical dilatation at the time of prolapse.

TABLE I. FETAL SURVIVAL

	LIVE BABIES	DEAD BABIES
Cervix fully dilated (or almost dilated)	36	9
Incomplete dilatation of cervix	7	19

It is obvious that the time factor and ease of prompt delivery were most important in securing a living child. It is of interest, therefore, to further study treatment of individual cases in two groups:

1. The group where dead babies were obtained in spite of full cervical dilatation: failure under relatively favorable conditions.

2. The group where live babies were obtained in spite of incomplete cervical dilatation: success under relatively unfavorable conditions.

It is obvious that in each of these instances the baby's condition before treatment of the prolapsed cord was so compromised or unpromising that no better result could be expected of any form of delivery.

This heterogeneous group permits no conclusions other than the recognition that good fortune may occasionally intervene when good judgment is lacking.

TABLE II. FULL CERVICAL DILATATION—DEAD BABIES

CASE NUMBER	TREATMENT	CONDITION OF BABY
2	Immediate breech extraction	Poor condition before treatment
24	Cord replaced; delivery with fundal pressure	Nonviable infant
25	Assisted breech	Nonviable infant
27	Pituitrin—spontaneous delivery	Nonviable infant
45	Immediate version and breech extraction	Poor condition before treatment
52	Immediate version and breech extraction	Poor condition before treatment
57	Cord replaced; attempted forceps at home (11½ lb. baby), later forceps extraction in hospital	Baby died before successful forceps delivery
63	Cord replaced; internal cephalic version and spontaneous delivery	Nonviable infant
64	Version and breech extraction; difficult operation for transverse presentation in tonic uterus	Infant probably dead before treatment



## THE TREATMENT OF ACUTE POSTPARTUM THROMBOPHLEBITIS OF THE LOWER EXTREMITY BY CONTINUOUS CAUDAL ANESTHESIA

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THE treatment of thrombophlebitis of the lower extremity is one of the most time-consuming and discouraging therapeutic measures attempted, particularly when handled by the traditional regimen of rest, elevation of the affected part, heat, and sedation. Heparin, dicumarin, penicillin, and sulfonamides are expensive, difficult of administration, dependent upon laboratory studies and control, or are only adjuvants to the so-called "conservative" or supportive treatment. However, if vascular inadequacy has become established, these medicaments will be of little or no value, and a confinement of six to eight weeks in bed followed often by years of swelling, pain, and disability confronts the patient.

Phlegmasia alba dolens, "milk-leg," or, more properly, postpartum femoroiliac thrombophlebitis is a catastrophe of the puerperium, and although much has been done in the prophylaxis of this complication, less has been accomplished in its treatment.

It is not within the scope of this paper to discuss all the causes of acute femoroiliac or femorosaphenous thrombophlebitis, nor are we concerned primarily with their prophylaxis or diagnosis here, important though they may be. Moreover, although it is recognized that not all early cases are clear-cut, that the complete, typical findings are not invariably seen, and that a phlebotrombosis must be ruled out, we shall consider only the therapy of definite, acute postpartum infectious vascular occlusion of the venous system of the leg by continuous caudal anesthesia.

### Pathologic Physiology of Thrombophlebitis

In 1934, Leriche and Kunlin<sup>1</sup> promulgated a theory of vasospasm in and about a vessel involved in a thrombophlebitic process. The vasomotor reflex, they indicated, originated in the irritated segment, involving the central nervous system, with a resulting upset of the normal intervascular relations. There were three phases involved in this process: (1) vasospasm—constant and most significant, (2) extension of the thrombus, and (3) arteriospasm. Leriche and others<sup>2-4</sup> reported numerous cases of thrombophlebitis all relieved by sympathetic nerve block following paravertebral injection of local anesthetics.

The development of the manifestations of thrombophlebitis, therefore, was on a basis of disturbed physiology, in a very large measure, rather than on an anatomic-pathologic foundation.

In 1939, Ochsner and DeBakey<sup>5, 6</sup> reported studies tending to prove that the evidence of pathology in the affected limb was not due to vasospasm so

4. If the infant has already succumbed at the time of recognition of the cord prolapse or it has been so badly compromised that the fetal heart cannot be improved with oxygen and elevation, it is unprofitable to subject the mother to major obstetric operations.

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### Continuous Caudal Anesthesia Technique

Hingson, Edwards, and Southworth's technique<sup>8, 11</sup> is the injection of 30 c.c. of (usually) 1.5 per cent metycaine in Ringer's solution into the sacral space through the sacral hiatus. A Hingson malleable 19 gauge 2½-inch or 3-inch needle is preferred. Twenty c.c. of the solution is injected per hour for four hours or more for prolonged effect. This cycle of four-hour treatment may be repeated once or more with interspaced "rest" periods, the needle being left in situ during the entire treatment. During this time, the patient is free to lie on the side or back with the legs elevated to 15°.

Complete relief of pain is reported within fifteen minutes after caudal injection, and no resumption of the discomfort is usually reported by the patient throughout the course of twelve or more hours of treatment. Simultaneous bed rest with slow, regulated exercise is naturally helpful in maintaining muscle tone with the prevention of extension of the thrombophlebitis. The patient is allowed up soon after the course of treatment, the local tenderness having disappeared altogether, with most if not all the edema. An elastic bandage or stocking has been recommended for a week or more, until vascular balance is re-established.<sup>10, 13</sup>

Ellis and Sheffery<sup>12, 13</sup> have added a series of 16 cases of pelvic thrombophlebitis to those (number not revealed) cases of femoral thrombophlebitis recorded by Hingson and Edwards.<sup>9</sup> Also, one case of acute femoroiliac thrombophlebitis, postoperative, cured by continuous caudal anesthesia is reviewed by Urschel and Salley.<sup>14</sup> These four reports are the only articles noted in the literature to date employing the continuous caudal anesthesia technique in such treatment. Not a single case of embolism has been reported following the institution of sympathetic nerve block by either the lumbar paravertebral or the caudal methods.

We have treated five cases of acute postpartum thrombophlebitis of the lower extremity (three deep-femoral and two extensive superficial-saphenous) by continuous caudal anesthesia with spectacular, prompt, and complete cure.

### Review of Cases

Table I briefly summarizes the clinical course of these five cases of thrombophlebitis, including the antepartum, intra- and postpartum complications contributing toward septic vascular occlusion.

We, together with others concerned with the problem of postpartum thrombophlebitis, are naturally vitally interested in its prophylaxis. However, it is apparent that neither will transfusions nor sulfa-penicillin therapy insure patients against phlebitis, nor will they cure many patients so affected. However, where these and certain other measures have failed, caudal anesthesia often appears to effect a cure (Cases 1, 3, 5).

Continuous caudal anesthesia was employed in a single course in one instance (Case 3), and in two courses in four patients (Cases 1, 2, 4, 5) in our study of therapy of thrombophlebitis of the lower extremity. Pontocaine and/or metycaine were used as anesthetic agents in all cases. The apparent variation was deliberate in an effort to test these long-acting drugs. However, the standardization of medication, dosage, and duration of treatment of thrombophlebitis by continuous caudal anesthesia are problems requiring further study before the optimum medication and a settled routine of therapy are established.

much as to arteriospasm, and that in some cases no inflammation or infection was apparent. In these latter cases, phlebothrombosis was the term employed.

Spasm, in thrombophlebitis, is a major cause of pain and edema. The normal passage of fluids from each capillary loop into the tissues is from the arteriole end, whereas, the return of the extracellular fluid into the vasculature, excluding the lymphatics, is via the venule end of the loop.

In the spastic vasculature of a thrombophlebitic extremity, the blood flow is diminished, the endothelium of the capillaries is altered by hypoxia and the excess catabolic products, and the permeability of the vascular walls is increased. Exudation of fluid occurs at this point and a collection of intercellular, perivascular edema fluid is the result. The resorption of this excess fluid is difficult, for the arterial pressure in the extremity is lowered, the venous pressure is increased, and the pumping effect of the arterial pulsation is minimized in a spastic system.<sup>5-7</sup>

Sympathetic nerve block not only relieves the vascular spasm but also the pain, and allows collateral circulation to become effective.

This greatly diminishes the permeability of the capillaries, markedly reduces the probability of the extension of the thrombus, relieves back stasis and facilitates the natural processes of resolution and repair.

Ochsner and his associates<sup>7</sup> popularized the paravertebral lumbar sympathetic nerve block in the treatment of cases of thrombophlebitis. After insertion of three to five needles and the injection of an anesthetic agent into the paravertebral space opposite L.1-5, complete relief of pain held for about one to two hours, and the leg became flushed, warm, and dry. Although complete relief of pain was rather temporary, the flushing of the extremity continued for a number of hours. The clinical course was generally: (1) immediately after injection—complete relief of pain with rarely three injections necessary; (2) within twenty-four hours—decline of temperature to normal in seventy-two to ninety-six hours; (3) reduction in edema in the first twenty-four to forty-eight hours with complete disappearance of swelling in seven to ten days (average four days).

Sympathetic nerve block, based on sound clinico-pathologic investigation and not empiricism, reduced the duration of illness in acute femoral thrombophlebitis from four weeks with supportive therapy to an average of four days!

Edwards and Hingson, in 1942,<sup>8</sup> developed continuous caudal analgesia in obstetrics, proving that the fractional or continuous principle of anesthesia, first suggested by Lemmon in spinal anesthesia, could be used over many hours for the control of pain. With caudal anesthesia, the sympathetic nerve fibers to the extremity running in the rami communicantes, and traveling with the sensory fibers of nerves are routinely blocked in the epidural space. Continuous caudal anesthesia was next used in the specific treatment of thrombophlebitis of the leg by these same investigators in 1943.<sup>9</sup> Thus, a single needle insertion technique was substituted for multiple insertions and the sympathetic block was continued for hours with, as Lull and Hingson report, "more efficient release of the vasospastic elements and with more prompt improvement in all signs and symptoms of thrombophlebitis."<sup>10</sup>

tion of the pain to the left groin and down the leg. Definite swelling and pain in the left groin had been noted for three days prior to admission. She had been placed on sulfadiazine (1.0 Gm. every 4 hours) two days prior to admission by her local physician. Penicillin was begun upon entry into the hospital (30,000 U. every 3 hours). After six days of sulfonamides and four days of penicillin therapy, the patient was unimproved. The abdominal pain was less, but an acute femoroiliac-femorosaphenous thrombophlebitis had developed. Instead of the temperature falling with chemotherapy, it had risen to 102° F. Edema of the leg and ankle (2+) had developed, and pain and gross nodulation in Searpa's triangle, with inability of the patient to move the blanched left leg, had resulted. Seven hundred and twenty thousand units of penicillin had been given and chemotherapy was abandoned.

The patient then received continuous caudal anesthesia with 0.15 per cent pontocaine (45 c.c., initial dose). Analgesia to the costal margin was continued for six hours, a "rest" period of six hours was allowed, and another six hours of caudal anesthesia administered with the needle left in the sacral hiatus through the entire eighteen hours of treatment.

A prompt and astonishing improvement resulted. The patient no longer experienced pain in the groin, though tenderness over the femoral vessels remained for twenty-four hours longer. The swelling disappeared, and gradually the temperature fell from 102° F. to normal in twenty-four hours, to remain so thereafter. The white blood count dropped from 14,000 to 6,600, and the sedimentation rate from 31 to 20 mm./hr. (Cutler) in four days. Disability was eliminated, and the patient was active in bed from the day after caudal anesthesia to ambulation two days later. She was discharged seven days after therapy, or twelve days following readmission, and was completely recovered. There were no complications or unpleasant reactions to caudal anesthesia.

### Therapeutic Results

Table II is a review of the relief of thrombophlebitis of the lower extremity following continuous caudal anesthesia therapy. Pain was dispelled in all cases immediately after the analgesia "take." Pain did not recur in the "rest" period, or prior to the second course of caudal anesthesia. Objectively, after the institution of caudal, the temperature fell to normal to remain so thereafter in twelve hours in two cases (Cases 2 and 5), and in twenty-four hours in three cases (Cases 1, 3 and 4). Edema (2+) was dispelled in Case 5, after only six hours of caudal analgesia (extensive superficial thrombophlebitis), although in a comparable instance (Case 4) with less edema (1+), thirty-six hours were required for swelling of the leg to disappear. Twenty-four hours after the institution of caudal, there was complete resolution of edema in three cases (Cases 1, 2 and 3) of deep thrombophlebitis. Thrombophlebitis (or other complications) did not recur in any case, and all five patients treated recovered completely—to be ambulatory in forty-eight to seventy-two hours.

### Discussion

We have noted that early, acute cases of postpartum thrombophlebitis of the lower extremity are most amenable to continuous caudal anesthesia. If allowed to run a chronic course, it is recognized that thrombophlebitis is followed by a perivascular fibrosis, and resultant edema cannot be easily resolved. Collateral circulation rarely can be established and pain persists as a sequel to the phlebitis.

TABLE I. CASES TREATED

PATIENT	ANTEPARTUM COMPLICATION	LABOR AND DELIVERY	POSTPARTUM COMPLICATION	PRECAUDAL THERAPY	THROMBOPHLEBITIS	CONTINUOUS CAUDAL ANALGESIA
1. L. H. #2316 32 years para i	Antepartum hemorrhage at 30 weeks; partial placenta previa	Spinal anesthesia, shock, version-extraction	Anemia, marked; febrile uterine sub-involution	64 Gm. sulfadiazine, 720,000 U. penicillin transfusions (3)	(Deep) acute right femoral; PP. 29 d.	6 hrs. pontocaine+ 6 hrs. "rest"+ 6 hrs. pontocaine
2. D. H. #6452186 S.M.H. 18 years para i	0	Term; spontaneous	0	0	(Deep) acute right femoral; PP. 7 d.	4 hrs. pontocaine+ 4 hrs. "rest"+ 4 hrs. pontocaine
3. B. J. H. #2581 30 years para iii	0	Term; spontaneous	Breast abscess, left	30 Gm. sulfadiazine	(Deep) acute left-femoral-saphenous; PP. 30 d.	8 hrs. pontocaine
4. M. E. #3265 29 years para iv	0	Term; spontaneous	0	0	(Superficial) acute, segmental (2). right long saphenous; PP. 3.d.	6 hrs. metycaine+ 6 hrs. "rest"+ 6 hrs. pontocaine
5. B. J. #3106 43 years "elderly primipara"	Myomata uteri; typical funnel pelvis; disproportion	Term; elective cesarean section classical	Anemia, moderate; low-grade febrile reaction; uterine sub-involution	400,000 U. penicillin transfusion	(Superficial) acute, almost entire long saphenous; Rt. PP. 13 d.	6 hrs. metycaine+ 6 hrs. "rest"+ 6 hrs. metycaine

One typical case (Case 1) is reported for illustration of the problems involved.

CASE 1.—L. H. No. 1924 and No. 2316. The patient was a 32-year-old, white, unregistered gravida i, with an unmeasured pelvis and a later reported negative Kahn. She was admitted to the Hospital in the thirtieth week of her pregnancy, not in labor, with the history of gross, painless vaginal bleeding. The patient was grouped and cross-matched. Vaginal examination revealed a partial placenta previa, with the cervix 2 cm. dilated but poorly effaced. A cesarean section was advised and she was prepared for surgery. The patient was given 4 c.c. of a 1.5 per cent metycaine in Ringer's solution as an initial dose for continuous spinal anesthesia. The injection was apparently an intravascular one and she sank into profound shock. After about one hour she had revived with plasma, blood, oxygen, and stimulants. The fetal heart remained good throughout and bleeding slackened. Section was abandoned and the membranes were ruptured artificially. Twelve hours later the patient went into spontaneous labor, again with brisk bleeding and recurrent shock. More blood was administered and, at 4 cm. cervical dilatation, a foot was brought down and a relatively easy version effected. The infant, a normal male weighing 5 pounds, was delivered soon after and survived. The mother, still in shock, improved after three transfusions and supportive therapy, but without sulfonamides. She left the hospital on the eleventh postpartum day recovered, though still slightly anemic. No gross lacerations had been sustained at delivery, and the temperature had been elevated (100.4° F.) only on the second postpartum day.

The patient was readmitted to the hospital nineteen days later because of severe, left lower quadrant pain beginning five days before. There was radia-

### Summary

1. The development and rationale of sympathetic nerve block by paravertebral and continuous caudal anesthesia in the treatment of thrombophlebitis of the extremity are reviewed.

2. Five cases of acute, postpartum thrombophlebitis of the lower extremity successfully treated by continuous caudal anesthesia are presented.

3. Continuous caudal anesthesia is a sound, simple, superior method of treatment in cases of acute thrombophlebitis of the lower extremity.

The opinions expressed here are those of the author and do not necessarily reflect those of the Navy Department.

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TABLE II. RESULTS OF CONTINUOUS CAUDAL ANESTHESIA

PATIENT	PAIN RELIEF (MIN.)	NORMAL TEMPER- ATURE (HR.)	LOSS OF EDEMA (HR.)	LOSS OF TENDER- NESS (HR.)	AMBULA- TION POST- CAUDAL (HR.)	RECUR- RENT THROM- BO- PHLE- BITIS	OUTCOME
1. L. H.	15	24	(2+) 24	24	72	0	Recovered
2. D. H.	15	12	(2+) 24	24	48	0	Recovered
3. B. J. H.	30	24	(1+) 24	32	48	0	Recovered
4. M. E.	15	24	(1+) 36	36	48	0	Recovered
5. B. J.	15	12	(2+) 6	24	48	0	Recovered

Since the vicious cycle of "pain-vascular spasm-pain" contributes most to the patients' debilitation, reduction in pain is followed by relief of vascular spasm and disappearance of edema. Pain, moreover, can be controlled completely, promptly, and for a prolonged period by the single caudal needle insertion.

We believe pontocaine and metycaine are nontoxic in the doses recommended and with the usual precautions. It is felt that the prolonged action of pontocaine is often desirable, since frequent injections are obviated. The level to which pontocaine may extend in the epidural space, however, is difficult to predict, and overdosage may occur unless the anesthetist is cautious. In our experience, metycaine is easier to control and the action is moderately prolonged. Furthermore, metycaine can be used for the skin anesthesia as well as for the test dose. We have not used procaine often, even though it is slightly less toxic, because of its brief anesthetic action.

We believe that a level of analgesia to L.1 is sufficient for the treatment of thrombophlebitis of the lower extremity by continuous caudal anesthesia. Using pontocaine 0.15 per cent or metycaine 1.5 per cent solution, approximately 30 c.c. (total initial dose, including an 8 to 10 c.c. test administration) with 20 to 25 c.c. as often thereafter as necessary (one to three hours) is sufficient to maintain analgesia at therapeutic levels. One or two cycles of treatment with the needle left in situ are recommended.

Anemia, hypotension, febrile state, and sensitivity to the anesthetic agent are all factors contributing to unpleasant side effects and possible shock. In our experience, nausea, vomiting, and shock did not occur. Barbitol analgesia, together with epinephrine, added ease and safety to the procedure.

The relaxation we have achieved, the relief of pain, and the continuation of effective therapy are not possible save by sympathetic nerve block, and are most profound with continuous caudal anesthesia, in the treatment of acute postpartum thrombophlebitis of the lower extremity. Hingson has indicated that in the metabolism of metycaine, a demerol-like, piperidine ring, may be the partial explanation for the added analgesia and slight euphoria noted with metycaine.<sup>15</sup>

In acute, fulminating cases of thrombophlebitis of the ilio-femoro-saphenous system, continuous caudal anesthesia should be considered the best method of therapy, and chemotherapy should be considered an adjunct.



TABLE I. SIGNIFICANCE OF DIFFERENCES BETWEEN MEAN FILTRATION RATES FOR CONTROL, NORMALLY PREGNANT, AND TOXEMIA SUBJECTS

GROUPS	DIFFERENCE BETWEEN MEANS	STANDARD ERROR OF DIFFERENCE	(K)*	P*	SIGNIFICANT DIFFERENCE
Control vs. normal pregnancy	0.037	0.009	4.15	0.0001	Yes
Controls vs. toxemic pregnancy	0.006	0.010	0.60	0.5485	No
Normal pregnancy vs. toxemic pregnancy	0.031	0.012	2.58	0.0099	Yes

Rates of filtration in c.c. per minute per 100 c.c. of forearm.

\*(k) is ratio of difference to its standard error. P is probability of the (k) magnitude being exceeded solely through errors of random sampling.

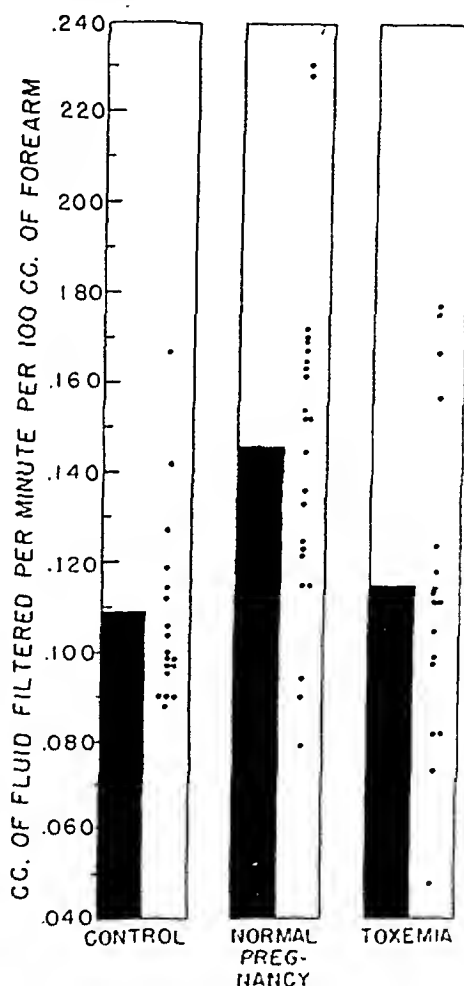


FIG. 1.— Rates of filtration in control subjects, normal pregnant women, and pregnant women with toxemia. The top of each solid column indicates the respective mean value.

still seem to indicate that, for the group as a whole, normally pregnant women permit the filtration of fluid from minute blood vessels into forearm tissues at a more rapid rate than do nonpregnant women or pregnant women with some form of toxemia of pregnancy. The precise mechanism of this phenomenon, granting the validity of the conclusion, cannot be satisfactorily explained on the basis of present knowledge, and nothing of importance can now be added

# FURTHER OBSERVATIONS ON CAPILLARY FILTRATION RATES IN PREGNANCY\*

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A PREVIOUS report<sup>1</sup> indicated that the filtration of fluid through the capillary wall proceeds in the latter weeks of pregnancy at a rate which is somewhat increased over the normal (nonpregnant). Women with toxemia of pregnancy did not exhibit this increase in rate of filtration, presumably because of considerable amounts of fluid already present in the tissues. Since publication of the first report in 1943, twenty-four additional subjects have been studied by the plethysmographic technique previously employed.<sup>1-5</sup> Eight of these were normal controls, eleven were normally pregnant near term, and five were pregnant with signs and symptoms of pre-eclampsia. The filtration rates in these new subjects have been combined with those previously reported, and statistics have been recalculated from the larger samples. While a few further observations were made on postpartum patients, these are not reported here because they add nothing of consequence to the figures already presented.

## Observations

1. *Normal, nonpregnant controls.*—In 20 normal women, ranging in age from 22 to 35 years, the mean rate of filtration of fluid from the minute vessels into the tissues of the forearm was  $0.109 \pm 0.004$  c.c. per minute per 100 c.c. of forearm. The range of individual values was from 0.088 to 0.167 c.c. per minute per 100 c.c. of tissue and the eight new observations all fell within the range obtained for the twelve original subjects (Fig. 1).

2. *Normally pregnant subjects.*—In 23 women (11 new observations) observed during the final eight weeks of normal pregnancies the mean rate of filtration was  $0.146 \pm 0.008$  c.c. per minute per 100 c.c. of tissue and the range was from 0.079 to 0.230 c.c. (Fig. 1). Although it is obvious from inspection of Fig. 1 that many individual values for the pregnant subjects fall within the range of control values, yet there is a statistically significant difference between the mean values of the two groups (Table I).

3. *Toxemic subjects.*—In 17 pregnant women (5 new observations) with either pre-eclampsia or arteriolosclerotic toxemia observed late in the last trimester the mean rate of filtration was  $0.115 \pm 0.009$  c.c. per minute per 100 c.c. of forearm, and the range was from 0.048 to 0.177 c.c. (Fig. 1). The average value was not significantly different from that of the controls, but it was *significantly lower* than that of the normally pregnant women. It should be noted that the two lowest individual rates of filtration were found in this group of toxemia patients.

## Discussion

The additional observations reported here do not alter in any way but merely substantiate the conclusions reached in the previous report.<sup>1</sup> The figures

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## CYSTIC ADENOMYOSIS OF THE UTERUS

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**A**DENOMYOSIS of the uterus is a well-recognized cause of pathologic hemorrhage and dysmenorrhea; the cardinal symptom, namely, menorrhagia or metrorrhagia, may occur without any complicating abnormality. Hemorrhage is explained by the endocrine dysfunction that exists. The endocrine dysfunction is manifested by a well-marked hyperplasia of the endometrium. Dysmenorrhea is explained by the invasion of the islands of endometrium which may cause painful contractions of the uterine musculature.

Adenomyosis is defined as the heterotopic occurrence of islands of endometrium into the uterine wall. It is a benign invasion of the endometrium into the uterine musculature, and is associated with a diffuse overgrowth of the musculature.

### Incidence

There is a great variability in the reports of the incidence of adenomyosis. Fallas and Rosenbloom<sup>1</sup> reported an incidence of 49.6 per cent in 260 cases of endometriosis. Counsellor,<sup>2</sup> in 884 cases of endometriosis, found an incidence of 69.6 per cent. Lewinski<sup>3</sup> reported that 53.5 per cent of all uteri removed at necropsy showed adenomyosis, and therefore called the findings mainly physiologic. Frankl<sup>4, 5</sup> disagreed with this high incidence. Over a ten-year period at the Alexander Blain Hospital<sup>6</sup> there were 73 cases of adenomyosis, representing an incidence of 10.7 per cent of all uteri removed. At the Royal Victoria Montreal Maternity Hospital, in 1944, there were 60 cases of adenomyosis in 236 uteri removed for various reasons, representing an incidence of 25 per cent of all uteri removed.

The age incidence varies from 25 to 50 years. It is usually found within the active sex life of an individual, but may be found in women past the menopause. Frank and Geist<sup>7</sup> studied a series of 203 cases of adenomyosis. In this group 23, or 11.3 per cent, were women past the menopause. Dreyfuss<sup>8</sup> reported an average age of 46 years for adenomyosis. Shamnakis<sup>9</sup> found that 90.6 per cent were between 30 and 60 years, and 53.6 per cent were in the fifth decade. Adenomyosis is a disease of the second half of the generative period, and there is usually a history of many pregnancies.

### Histogenesis

The pathologic diagnosis of adenomyosis rests on the demonstration of epithelial and stromal elements closely resembling the endometrium within the uterine musculature. Numerous theories have been postulated to explain the origin, and it would appear from a review of these theories that no single mechanism is universal in the pathogenesis of the disease.

### Theories

1. Cullen,<sup>10</sup> and Frankl<sup>4, 5</sup> postulated a theory of direct invasion of the uterus by normal endometrium. The stroma of ectopic islands derived from the mucous membrane prepares the way for glands to follow. In this connection it is interesting to note that, in 1923, Robert Meyer<sup>11</sup> showed that the stroma of endometrial islets destroys the myometrium. Destruction is not

to the discussion presented in 1943. The obvious inference is that the permeability of the capillary wall is for some reason increased in the pregnant woman, at least in the face of intracapillary pressures which are above the normal range. However, despite the comparative ease with which fluid leaves the vessels in the pregnant patient, some mechanism seems to be operating to retain fluid within the vascular system under normal circumstances. If this were not so, one would expect to find generalized edema much more commonly in association with normal pregnancy. With respect to the mean filtration rate in the toxemic group and the very low individual values observed in these subjects, it might simply be pointed out again that filtration is diminished in the presence of elevated tissue pressures built up by pre-existing edema fluid. One would predict, then, a comparatively low rate of filtration for the toxemic patient with an already established generalized edema. In other words, the plethysmographic technique used in this study is not helpful in determining whether the capillaries of toxemic patients are more permeable than usual, as might be postulated, since filtration has preceded the experimental observations and the *rate* of further transfer of fluid is necessarily diminished. For a complete discussion of the relation of tissue pressure to filtration rate, the reader is referred to the fundamental paper by Landis and Gibbon.<sup>3</sup>

### Summary and Conclusions

Twenty-four additional observations on the rate of filtration of fluid through the capillary wall, obtained with a pressure plethysmograph, have been combined with figures previously reported and new statistics have been computed. The more recent values tend to corroborate the previous conclusion that the rate of filtration through the capillary wall is somewhat increased over the normal in the last eight weeks of normal pregnancy. No satisfactory explanation for this finding is presently available. Patients with toxemia of pregnancy do not exhibit this increase in rate of filtration, presumably owing to the fact that they have sufficient edema to interfere to some extent with further filtration of fluid into the tissues.

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## Case Reports

Two cases of cystic adenomyosis from the gynecologic department of the Royal Victoria Montreal Maternity Hospital are presented. These are outstanding because of the large size of the cysts.

CASE 1.—A para 0, aged 36 years, who was admitted with complaints of dysmenorrhea which had become severe for the last six months; and menorrhagia of six months' duration. Family history and personal history were nonecontributory, except that she had a complete abortion at two months in 1939. The dysmenorrhea was premenstrual in time. The menstrual periods started at 14 years of age, were regular every 26 to 28 days, and lasted 2 to 3 days. The menorrhagia was manifested by profuse flow which was prolonged to five days for the last six months. Physical examination revealed a normal, healthy, and well-developed woman. Pelvic examination showed a nulliparous, healthy vulva and vagina. The cervix was edematous, the external os circular and healthy. The uterus was anteverted, anteflexed, mobile, and irregularly enlarged to the size of a three months' pregnancy. The appendages were normal on palpation.



Fig. 1.—Cystic adenomyosis, low power (X20).

On June 16, 1945, a supravaginal hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were performed. The uterus was grossly irregular and measured 15 by 9 by 7 cm., the seat of intramural fibromyomas. Both ovaries were slightly enlarged and cystic. The pathologic examination revealed a large cystic space in the myometrium (Fig. 1) which was lined by typical endometrial cells of low columnar variety. The rest of the microscopic examination revealed a premenstrual endometrium, fibromyomas uteri, and follicle cysts of the ovaries.

CASE 2.—A para iv, aged 32 years, who was admitted with complaints of menorrhagia and dysmenorrhea for six years. Before her last pregnancy in 1939 her periods were regular and normal, lasting five days. Menarche started at 12 years of age. Gradually, since 1939, menorrhagia had become marked, and the flow lasted between fourteen to twenty-one days each month. Dysmenorrhea with radiation of pain to the lumbosacral region had become severe.

restricted to the interstitial tissue but involves the muscle cells, i.e., the myofibrils which are responsible for the function of muscle. The most aggressive types of adenomyosis are those with a very cellular stroma. Frankl has shown that there exists a continuation of the mucous membrane beyond its normal border line. Adenomyosis is not related to any inflammation.

2. Cullen:<sup>10</sup> The islands of ectopic endometrium represent misplaced remnants of the Müllerian duct epithelium.

3. von Recklinghausen<sup>12</sup> and Pfannenstiel:<sup>13</sup> The epithelium originates from the mesonephric tissue of the Wolffian duct.

4. Iwanoff<sup>12</sup> and Novak:<sup>14</sup> Adenomyosis arises from the activation of celomic rests.

5. Meyer:<sup>15, 16</sup> Adenomyosis arises from epithelial heterotrophy dependent on an inflammatory or hormonal stimulus.

6. Adenomyosis is a result of fetal budding of the epithelium, or represents misplaced islands of fetal mucosa.

7. Halban,<sup>17</sup> Bertner,<sup>18</sup> and Sampson:<sup>19-22</sup> Adenomyosis is a result of lymphatic or hematogenous spread of endometrium, i.e., metastatic deportation of glands. Fragments of endometrial tissue may be disseminated into the venous circulation during menstruation from the mucous membrane lining the uterus. This endometrial tissue, set free by menstruation, may continue to grow if transported to a favorable environment.

8. Brines and Blain<sup>6</sup> suggested that adenomyosis was a result of spontaneous generation of endometrial stromal or interstitial cells from and within the myometrium. They advanced the theory that by a process of dedifferentiation or metaplasia, cells less mature but highly specialized were produced. These cells possessed the potentiality to differentiate into epithelial cells, which formed endometrial glands. The process was comparable to the differentiation of fibroblasts into osteoblasts and chondroblasts. The stromal cells were formed before the glands. This was borne out by the fact that small islands of stromal cells were encountered which, by serial section, were found to be unassociated with gland formation.

### Pathology of Adenomyosis

The gross characteristics of adenomyosis reveal a slightly or markedly enlarged uterus due to a diffuse overgrowth of the musculature that is part of the lesion of adenomyosis. The enlargement is usually diffuse and symmetrical, but asymmetrical enlargement may be a feature when there is irregular distribution of the islands of endometrium. On section the gross surface reveals a trabeculated appearance, but there are no circumscribed nodules as seen in myomas. There are indefinite nonencapsulated areas of hypertrophied smooth muscle bundles. There are dark hemorrhagic or chocolate-colored areas which vary from a few millimeters in diameter to large cystic spaces several centimeters in diameter. Large cysts, however, are rare. The microscopic cysts and islands of tissue are scattered discretely through the musculature. Adenomyosis ranges from minute incursions of endometrium to extensive foci far removed from the endometrium. In the majority of cases the ectopic endometrium is situated in the inner half of the uterine wall and often communicates with the mucosal layer.

The pathologic diagnosis is based on the microscopic findings of endometrial islands of glands and stroma within the uterine muscle. The ectopic foci show the typical histologic gland and stroma structure. There are wide variations in regards to the functional state of the endometrium. Complete cyclical changes may be revealed, but usually the ectopic areas respond only to estrogenic stimulus. Thus the aberrant tissue seldom shows secretory activity. Actual bleeding into the glands seldom occurs. In many cases there is an associated endometrial hyperplasia.

larged to the size of a seven weeks' pregnancy. The appendages were clear. On May 19, 1945, a 600 c.c. blood transfusion was given. On May 21, 1945, the hemoglobin was 63 per cent; red blood cells, 3,500,000; platelets, 210,000; prothrombin time, 45 seconds; fibrin time, 2 minutes, 10 seconds; complete coagulation, 11.5 minutes.

On May 28, 1945, total hysterectomy was performed. The Fallopian tubes and ovaries were healthy and were not removed. The uterus measured 15 by 10 by 8 cm. On section, in the region of the fundus, an intramural cyst 3.5 cm. in diameter and filled with sanguinous fluid was discovered. This cyst communicated with a smaller cyst 1.5 cm. in diameter. Circumscribed nodules were present throughout parts of the uterine wall. The cervix on section showed dilated cervical glands.

Microscopic examination of the cysts described in the gross revealed that they had a lining architecture of typical endometrium, glands, and stroma. These are represented under low and high magnification in Figs. 2 and 3. The rest of the pathologic examination showed cystic cervicitis, polypoid hyperplasia of the endometrium, and fibromyomata uteri.

While adenomyosis is a common pathologic entity today, the finding of macroscopic cystic adenomyosis is rare and worthy of note. It would appear that these cysts could arise either from misplaced remnants of Müllerian duct epithelium or as a result of lymphatic or hematogenous spread into the uterus.

### Summary

1. The history, incidence, and histogenesis of adenomyosis are reviewed and brought up to date.

2. The pathology of adenomyosis is described and the important features, viz., ectopic endometrium and diffuse overgrowth of the musculature, stressed.

3. Two cases of macroscopic cystic adenomyosis are described and the microscopic pathology is presented.

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Her last period lasted five weeks. Family history and personal history were noncontributory. Physical examination revealed a thin, pale, white female. Blood determination on May 17, 1945, showed a hemoglobin of 54 per cent, white blood count of 10,500, and a sedimentation rate of 38 (23 conjugata vera) mm. Fasting and postprandial sugars were 96, and 119 mg. per cent, respectively. Pelvic examination revealed a normal parous vulva and vagina, and a firm, healthy cervix. The uterus was anteverted, anteflexed, and en-

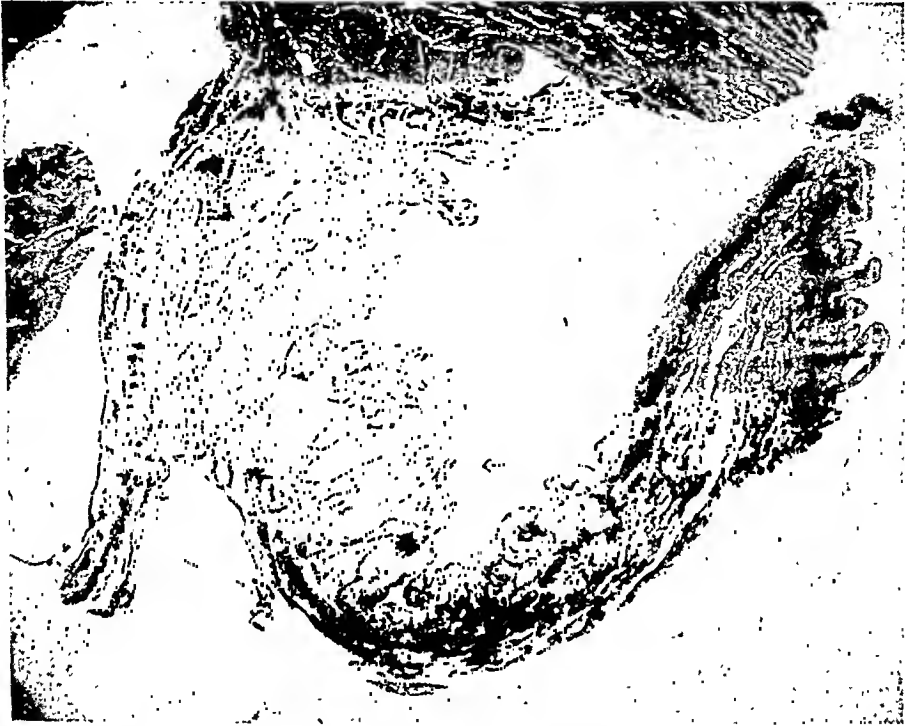


Fig. 2.—Cystic adenomyosis, low power ( $\times 20$ ).

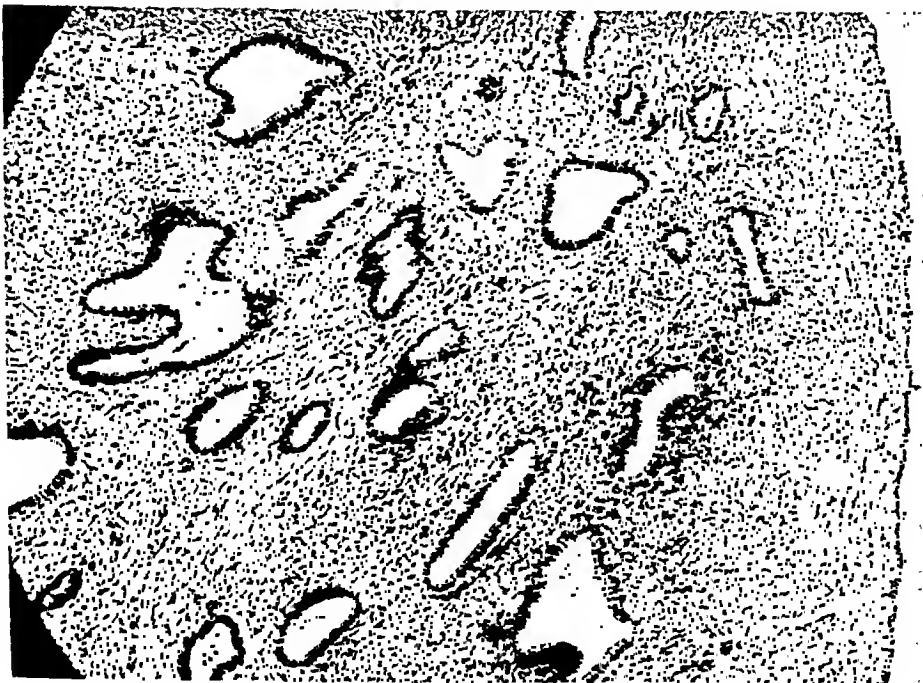


Fig. 3.—Cystic adenomyosis, high power of Fig. 2 ( $\times 400$ ).



The greater part of the tumor was composed of neuroglia. The glia cells had scant cytoplasm, the processes often were numerous and short. In some areas the glia cells were more compactly arranged. The areas composed of nervous tissue were usually surrounded by fibrous tissue, rather poor in nuclei and blood vessels, and having in some regions a gyrus-like structure (Fig. 1). There were, however, neither typical layers of ganglion cells nor "subcortical" formations of white substance. In other parts were ganglion cells of different shapes and everywhere appearing fully mature. They had the typical large nucleus with nucleolus and axones as well as dendrites in varying numbers (Fig. 2). Sometimes they were also apolar, pyramidal, or round. Myelin sheaths were nowhere to be found.



Fig. 1.—"Gyrus"-formations of the nervous tissue (large tumor of the right ovary) ( $\times 172$ ).

Considering the irregularity of the nervous tissue, it was surprising to find a completely developed cerebellar cortex in the upper pole of the tumor. There was, corresponding to the normal, an internal granular layer, a single layer of Purkinje cells, and an external gray substance with capillaries arising from the leptomeninges (Fig. 3).

Occasionally there appeared a few sympathetic ganglia. Bundles of normal-appearing nerve fibers occupied larger areas of the tumor. Less numerous were proliferations of the neuroepithelium, irregularly shaped tubules lined by high cylindrical epithelium. As often described in teratomas there were numerous choroid plexuses to be seen.

The small, enucleated tumor contained fat tissue that was covered by skin and its appendages. In addition, there were a few smaller cysts lined by melanin-containing cells, one small island of cartilage, and a few small bundles of smooth muscle fibers.

The piece of omentum contained well-circumscribed ovoid and irregularly shaped nodules of neuroglia. The latter was rather poor in cells and located among the fat tissue of the omentum. In some regions these nodules were very numerous, so that almost no fat tissue was to be seen. Ganglion cells and neuroepithelium were absent. Here and there a few groups of small round cells were present. In some areas they appeared more densely arranged and here their shapes were somewhat irregular.

# SOLID TERATOMAS OF THE OVARY WITH NEUROLOGICAL METASTASES

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**I**F MALIGNANT changes occur in solid teratomas of the ovary, they are seen almost exclusively in elements of the nervous tissue, and in those of the digestive or of the respiratory tract.<sup>1, 2, and others</sup> Peritoneal implantations of nervous tissue derived from an ovarian teratoma, however, are apparently rarities. Only ten such cases have been reported.<sup>3-10</sup> It was, therefore, deemed worth while to present one more case, and to compare the histologic characteristics and clinical behavior of the group.

## Case Report

A 22-year-old woman complained of abdominal pains and swelling of the abdomen for four months. Physical examination revealed a soft, cystic tumor filling the entire pelvis and extending from the right lower quadrant toward the left upper quadrant. The uterus was not palpable. Abundant colostrum was present in both breasts. The Asehhheim-Zondek reaction was negative. Upon laparotomy there was found considerable ascites. The greater omentum was covered with numerous whitish, opaque nodules approximately 2 mm. in diameter; it was attached to a tumor of the *right* ovary. This tumor was of elastic consistency extending upward to the spleen. After its removal another tumor of the *left* ovary was found and extirpated. The latter was somewhat larger than a man's fist. Its surface was smooth and whitish-yellow in color. A piece of omentum was removed for histologic examination. After having x-ray treatment the patient was observed and in good condition for fifteen months post-operatively.

The tumor of the right ovary measured 22 by 19 by 10 cm. after being fixed in 10 per cent formol. It weighed 1,750 Gm. and was completely surrounded by a grayish fibrous capsule. In general, the tumor was nodular and firm in consistency; some of the nodules were gray, others were yellowish-gray. In one area was a tense translucent cyst. The cut surface was gray, and numerous fibrous septa divided the tumor into nodular masses of varying size. Scattered throughout the tumor were numerous cysts measuring as much as 1 cm. in diameter. Some of them contained clear gelatinous fluid. The Fallopian tube of this side could not be found.

A nodule composed of fat tissue and covered by skin and hair had been enucleated during the operation. It was about 2 cm. in diameter.

The piece of omentum was infiltrated by abundant whitish, faintly lustrous nodules, measuring 2 mm. in diameter.

The tumor of the left ovary was ovoid in shape, measuring 10 by 7 by 6 cm. It was composed of two communicating cysts. Attached to it was the unaltered Fallopian tube. One of the cysts was empty, the other contained sebaceous material and light brown hair. After the removal of the sebaceous material a plug the size of a hazelnut became visible in which bone particles could be palpated.

*Histologic examination.*—Tumor of the right ovary: About  $\frac{1}{6}$  of the tumor consisted of fat tissue, the other  $\frac{5}{6}$  was mainly composed of nervous tissue. There were also irregularly shaped small and minute islands of hyaline cartilage, rather cellular, and surrounded by a capsule of fibrous tissue. Next to these islands were mucous glands, arranged either singly or in small groups. There were small pieces of lamellar bone with fibrous bone marrow and nearby cysts of varying structure and size, mostly round, sometimes irregularly shaped, situated partially within the nervous tissue. Adjacent to some of these cysts were a few sebaceous glands and single hairs.

able. Rarely, one of the numerous sections showed the well-known pictures of the neuroepithelial tubules with their high cylindrical lining. Embryonal neuroglia was entirely absent. There were also histologic gyrus-like formations of the nervous tissue, and in the upper pole of the tumor a perfectly developed cerebellar cortex with leptomeninges.

There are 10 cases of neuroglial metastasizing ovarian teratomas reported in the literature.<sup>3-10</sup> Including the case presented they have some points in common. The age of the patient, 11 to 38 years, corresponds to that which Miller<sup>11</sup> and others generally give as the period when ovarian teratomas are most frequent. The site of the tumor is predominantly unilateral. In one case (v.Bary<sup>6</sup>) both ovaries were affected successively with an intervening interval of six months. The case presented here shows the rare combination of a solid teratoma of one ovary with a dermoid cyst of the other. The size of the tumor is generally considerable ("a man's head,"<sup>12</sup> "larger than a man's head,"<sup>13</sup> "watermelon,"<sup>17</sup> "a uterus in the seventh month of pregnancy,"<sup>18</sup> "half as large again as a man's head"<sup>17</sup>). As a rule, there is more or less abundant ascites. The metastases mentioned in these cases are exclusively implantation metastases. They are situated on the parietal and visceral peritoneum and omentum and appear as multiple, miliary ("small" and "minute") nodules or "vesicles" ("as in tuberculosis") of whitish or gray tissue, gelatinous, glassy, translucent, or opaque.<sup>3, 4, 5, 6, 10, and our case</sup> Moreover, there are also larger nodules, even up to the size of an infant's head.<sup>7, 9</sup>

What is of most interest is the histologic structure of these peritoneal metastases, particularly with regard to their relation to the primary tumor. All primary tumors prove their teratoid characters by their histologic composition; yet the predominance of the elements of the nervous tissue indicates their ability to proliferate. There are almost everywhere fully mature elements of the nervous tissue, except for neuroepithelial proliferations. The latter may be very marked and may even resemble an adenocarcinoma.<sup>7</sup> The ectodermal and entodermal components of the tumors show the same lack of embryonal forms.

The formation of typical cerebellar cortex, as found in the upper pole of the tumor reported here, should be particularly stressed. Willis<sup>12</sup> and Bettinger<sup>13</sup> described recently two solid teratomas of the ovary with equally well-developed cerebellar cortices. Askanazy<sup>14</sup> briefly mentioned a third case, but gave no detailed description.

At other times the nervous tissue may occur in the form of microscopic gyri (Buettner<sup>5</sup> and the case reported) or it may be highly differentiated with layers of ganglion cells and remnants of leptomeninges.<sup>7, 8</sup> Most prominent among the nervous tissue is the neuroglia. It is fully mature in nearly every case. Exceptions are v.Bary's<sup>6</sup> and Schairer's<sup>9</sup> cases. The former mentions neuroglia of "marked malignant character," the latter describes "immature" elements of nervous tissue.

Comparing the primary tumors with the peritoneal metastases, the latter were by far more uniformly constructed. They were almost exclusively composed of neuroglia and were well differentiated in five of the ten cases. Fleischmann<sup>3</sup> emphasized its embryonal structure, Neuhaeuser<sup>4</sup> and v.Bary<sup>6</sup> report its resemblance to round-cell sarcoma; in Ruzieska's case III<sup>7</sup> there was found a combination of cellular neuroglia with glandlike proliferations of epithelial tubules, and Schairer<sup>9</sup> describes cartilage and bone intermingled with mature and immature neuroglia.

The question arises, does the histologic structure of the primary tumor or of the metastases determine the clinical course? Of the eleven cases, the patient's fate is "unknown" in two.<sup>7</sup> Consequently, there are nine cases remaining to answer the above question. In five cases, including the case presented, the

Sections through the plug of the dermoid cyst of the left ovary showed cornifying stratified squamous epithelium, sebaceous glands, sweat glands, with dilated lumina, hair follicles, bundles of smooth muscle fibers, and cartilage. In addition, there were a few islands of neuroglia, small nerve fibers, and one sympathetic ganglion.

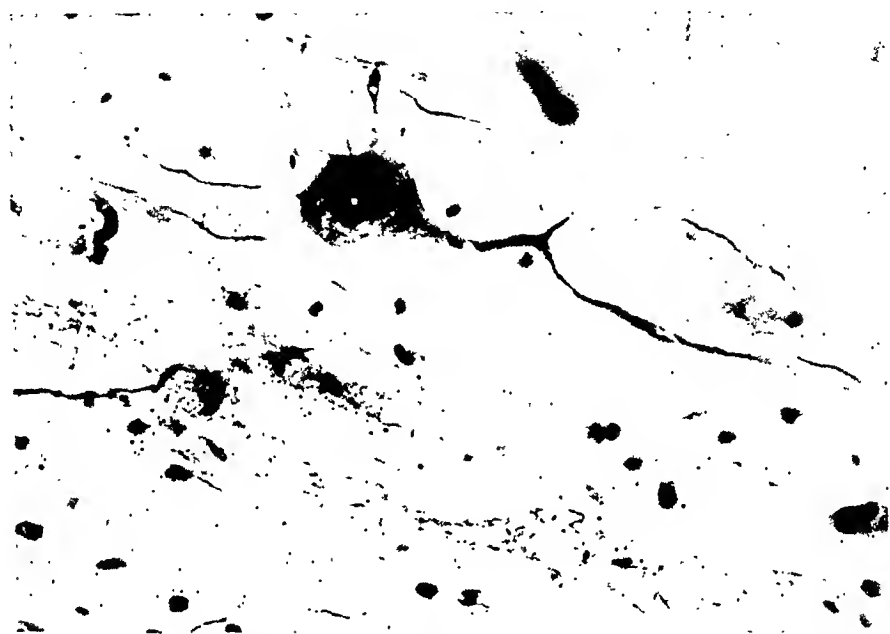


Fig. 2.—Multipolar ganglion cell (large tumor of the right ovary) ( $\times 662$ ).



Fig. 3.—Cerebellar cortex (upper pole of the large tumor of the right ovary) ( $\times 172$ ).

### Discussion

The above-described case offered a few peculiarities. There was a combination of a simple dermoid cyst (cystic teratoma) of one side with a solid teratoma of the other ovary that gave rise to metastases. Furthermore, the small amount of neuroepithelial tissue within the giant complex of nervous tissue was remark-

## BILATERAL SIMULTANEOUS TUBAL PREGNANCY

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THE infrequency with which one comes in contact with bilateral tubal pregnancy in the literature for the past ten years impresses upon one the rarity of this condition. When an authentic case is encountered in an Army General Hospital which has only a small Women's Surgical Section, it is likely to attract more than the usual amount of attention.

This patient, Mrs. Mabel P., aged 21 years, the wife of an Army sergeant, was brought to the Oliver General Hospital in an automobile by her husband at about 10:30 P.M., on March 6, 1946. She stated that she was at a dance, and after dancing about ten minutes she experienced a severe pain in her left lower quadrant. This pain very quickly became generalized throughout her abdomen. She became nauseated, vomited, and subsequently fainted. After she had been revived, she noted a small amount of vaginal bleeding. She was brought to the hospital immediately.

On admission, her pulse rate was 80, respiration 15, and temperature 97.8° F. She was seen by the Surgical Officer of the Day who believed she had a threatened abortion. Morphine, an ice cap to the abdomen, and the Trendelenburg position were ordered.

She was seen by the gynecologist on the morning after admission. Pain in both shoulders, generalized abdominal pain, faintness, and weakness were her chief complaints at this time. She stated that her last menstrual period had been January 15, 1946. Previous to this time she had always been regular. In the past two or three weeks she had experienced some enlargement and soreness of her breasts. Also, she had morning nausea on several occasions. She had had one previous pregnancy which terminated two one-half years ago with a normal delivery. A moderately severe toxemia accompanied this pregnancy. She gave no history of any abortions or miscarriages.

The physical examination revealed a well-developed woman who was very pale, had an anxious look on her face, and appeared acutely ill. The skin was moist and clammy. The conjunctiva and buccal mucous membranes were very pale. The breasts were moderately firm, with Montgomery glands present. There was an increase in the secondary areolar tissue. Her pulse was regular, thready, and the rate was 152. The blood pressure was 80/42. While making preparations to administer intravenous fluids, the systolic pressure dropped to 60. There were no murmurs, thrills, or enlargement of the heart. The lungs were clear.

period of observation extended two years—a comparatively short period. The other four cases ended in death (Fleischmann,<sup>3</sup> Schairer,<sup>9</sup> Ruzicska,<sup>7</sup> v.Bary:<sup>8</sup> four and twenty-four months after the first symptoms, seven and nine months after operation, respectively). In these four cases, some metastatic nodules had to be left on the peritoneum. This, however, is unimportant, for there was abundant tumor tissue left in five cases<sup>4, 5, 6, 10, our case</sup> that remained free from any recurrence of the tumor. Apparently the metastatic nodules may undergo regressive changes after removal of the primary tumor.

In the four fatal cases, the histologic descriptions of the tumors indicated definite derivatives from normal tissue. Fleischmann<sup>3</sup> characterized the neuroglia as “embryonal,” Ruzicska<sup>7</sup> described in his second case the proliferations of the ependyma as “resembling an adenocarcinoma,” v.Bary<sup>8</sup> recorded a “glioblastic sarcoma,” and Schairer<sup>9</sup> “immature” neuroglia at autopsy. Consequently, it would appear that any marked cellularity of the nervous tissue in the primary tumor or in the metastases would indicate an unfavorable clinical course. The “glioblastic sarcoma” represents a special form of malignant change occurring in the teratoma of the ovary. It may, however, be stated that the clinical behavior of ovarian teratomas with neuroglial metastases on the peritoneum corresponds to the doubtful clinical course of solid teratomas in general.

### Summary

To ten solid teratomas of the ovary with neuroglial metastases on the peritoneum reported up to the present, one has been added that contained fully developed cerebellar cortex and that was associated with a dermoid cyst of the other ovary. The neuroglial metastases from solid teratomas of the ovary are dissemination metastases on the peritoneum. They consist almost always of pure neuroglial tissue. In exceptional cases there may be proliferating neuroepithelium, cartilage, or bone among the neuroglia. The nervous tissue of the primary tumor may be highly developed (ganglion cells of various mature types; ganglion cells arranged in layers with remnants of meninges; gyrus formations; cerebellar cortex). The neuroglia in both primary tumor and the metastases may be fully mature, of an “embryonal” type, resembling a round-cell sarcoma, or of marked malignant character similar to a glioblastic sarcoma. According to the clinical observations, the neuroglial metastases of mature tissue seem to degenerate and disappear after extirpation of the primary tumor. Extremely cellular or immature neuroglia in the primary tumor or in the metastases may give rise to recurrences, and finally cause death.

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two one-half hours after the patient returned to bed. When she returned from surgery, her blood pressure was 140/60 and her pulse rate was 124. Nasal oxygen was started, and an ice bag was placed on her abdomen. One and one-half hours after operation the patient was rational and vomited about 30 c.c. of dark fluid. Two and a half hours later the patient roused and voided 180 c.c., and then went back to sleep and rested quietly until morning.

There was a gradual rise in temperature until the afternoon of the second postoperative day when it reached 104° F. At this time 1,000 c.c. of 10 per cent glucose were given intravenously, and 30,000 units of penicillin every three hours was ordered. The penicillin was continued until the patient had a total of 630,000 units and the temperature became normal.

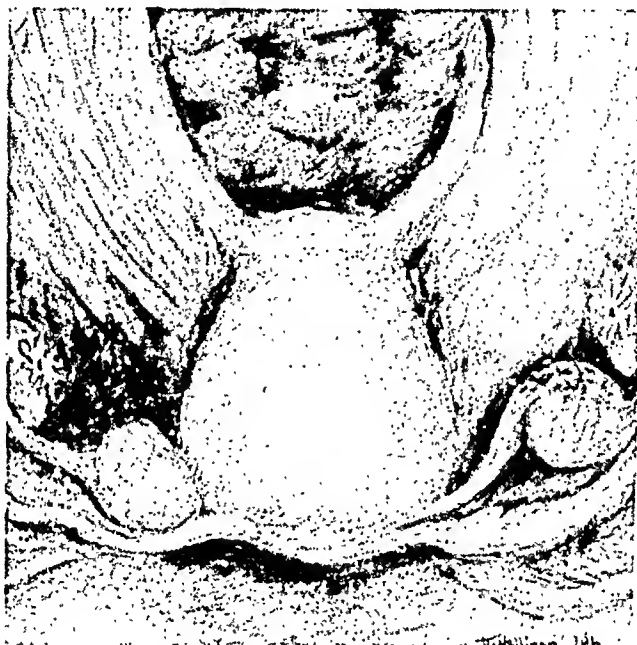


Fig. 1.

On the sixth postoperative day, the patient developed a very large herpes simplex which involved her upper lip, both ala nasae, and the right eyelid. These lesions were treated conservatively with zinc oxide ointment. The day following operation a catheterized urine specimen revealed the same findings as the preoperative specimens but a specimen on the second postoperative day was negative for albumin, and microscopically showed only 5 to 7 white blood cells per high power field. Four days postoperatively the urea nitrogen was 14 and the creatinin was 1.6. On the eighth day the skin sutures were removed and her incision had healed well. The patient was allowed out of bed on the tenth day and was discharged on the thirteenth in good condition. She was last seen twenty-three days after operation and at this time was asymptomatic. The incision had healed well and there was no herniation. The urinalysis and blood count, repeated at this time, was normal. The red blood count was 4,490,000.

The abdomen was moderately distended, and there was extreme tenderness throughout, most marked in the lower quadrants. No masses could be felt. A definite fluid wave was present. There was shifting dullness to percussion and moderate muscular rigidity throughout the abdomen, as well as rebound tenderness. Loud peristaltic sounds were heard in all areas.

The pelvic examination revealed a firm perineum. The cervix was exquisitely tender to manipulation, and slightly softened. Visualization showed some bluish discoloration. Due to the patient's extreme tenderness, the uterus and adnexæ could not be satisfactorily outlined. However, after she had been anesthetized for operation, a thickening of the uterine end of the right tube and a fullness in the left adnexa could be felt. However, no discrete masses could be demonstrated.

Immediately following the examination, 1,000 c.c. of 10 per cent glucose in normal saline was given intravenously. This was followed by 500 c.c. of whole blood. The blood pressure responded rapidly to this treatment.

An uncatheterized urine specimen, which had been taken earlier in the morning, showed a 4 plus albumin. The microscopic examination revealed many epithelial cells, granular casts, and a few white blood cells. Essentially the same report was later received on a catheterized specimen. A white blood count done at the time of the first urinalysis showed 44,950 leucocytes. The complete blood count report received later showed a 70 per cent hemoglobin, 3,330,000 red blood cells, and 43,700 white blood cells with the following differential count; neutrophils 83 per cent, lymphocytes 16 per cent, and monocytes 1 per cent. The N.P.N. at this time was 31.5 milligrams.

After the administration of intravenous glucose and blood, the patient's blood pressure reached 100/62, and the pulse rate was approximately 112 per minute. It was then thought that the patient was sufficiently out of shock to tolerate an anesthetic and laparotomy.

*Operation.*—The vagina was prepared, and a 17 gauge needle was inserted in the cul-de-sac. Some old, free blood was obtained. The abdomen was then opened in the midline. Before opening the peritoneum, it was noted that this tissue had a typical bluish color. When the peritoneal cavity was entered, a large amount of old, free blood, and many large clots were found. About 1,500 c.c. of blood and the clots were removed. A ruptured ectopic pregnancy, bleeding freely, about one one-half inches long and one inch in diameter was found in the middle third of the left tube. An unruptured ectopic pregnancy of approximately the same size was found at the uterine end of the right tube. Both tubes, including the pregnancies, were excised. The peritoneum was closed with plain catgut and the fascia with doubled No. 1 chromic catgut. The skin was closed with three silkworm gut tension sutures and silk. On several occasions during the operation the patient had a fall in blood pressure and a rise in pulse rate. In order that the operation could be completed as quickly as possible, no additional exploring was done.

While on the operating table, an additional 500 c.c. of whole, fresh blood was started. This was given slowly and was completely administered about



# ANCYLOSTOMIASIS AND HYPOPROTEINEMIA COMPLICATED BY PREGNANCY

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**D**ESPITE the fact that much has been written about the various anemias of pregnancy, a review of the literature reveals that little has been published regarding hookworm anemia, complicated by pregnancy. Although ancylostomiasis was common on Guam, the following case proved to be the most interesting, by far.

## Case Report

The patient (C. R. C.), a 23-year-old, unregistered, single Chamorro woman was admitted to the Military Government Hospital on May 20, 1945. Despite the patient's protests to the contrary, her kinsmen called the ambulance because they felt she appeared to be ailing sufficiently for hospitalization. Upon arrival at the hospital, the patient walked into the ward. Her complaints were slight dizziness, pain in the region of the mons pubis, swelling of the legs which began two weeks prior to admission, and amenorrhea for five months (the last menstrual period was December, 1944). In spite of the fact that the edema extended upward over the entire body, the patient had continued to perform all of her household duties. She had had no stool examination since 1940, nor had she taken helminthogogues. During the Japanese occupation her diet consisted chiefly of rice, fruits, and vegetables, since meat and milk were not available. After the Americans regained Guam, canned meats and powdered eggs were accessible, but the patient stated that she had consumed little of either.

*Physical Examination.*—The temperature was 98.8° F.; pulse 100; respirations 32; blood pressure 140/88. The patient was extremely pale and presented a generalized edema which pitted deeply on any part of the body. The eyelids were swollen almost closed. The patient seemed to be mentally sluggish and was virtually amnesic of the past few weeks.

The face was very swollen and waxy in appearance. The mucous membranes of the eyelids and mouth were extremely pallid. The tongue was pearly white and flabby. There were no cardiac murmurs or arrhythmias. The lung fields were essentially negative; only a few moist râles were elicited at the bases, posteriorly. The breasts were moderately enlarged, and a small amount of colostrum could be expressed from the nipples.

There was a four-plus pitting edema over the entire abdomen, particularly over the mons pubis. The uterus extended one finger's breadth above the umbilicus. The fetal heart tones were distant and rapid. The skin over the lower part of the abdomen showed many pallid striae gravidarum. Pelvic examination was deferred because of the severe edema of the labia.

The skin was dry, pasty in appearance, and tense. There was a four-plus pitting edema of the lower extremities. The fingernails were colorless. The deep tendon reflexes were sluggish. The impression was that the patient had ancylostomiasis and hypoproteinemia, associated with a 22 weeks' gestation.

*Laboratory Findings.*—The blood drawn from the right antecubital vein resembled cloudy serum streaked with strands of brick-red dust. The very few red cells present rapidly precipitated to the bottom of the test tube. The hemoglobin determination (Sahli), done from blood drawn from the vein, was not recordable—"less than 2 grams." The red blood cell count was 240,000. The white blood cell count was 400. A differential count was impossible because the blood smear

The following pathologic report was received from the laboratory:

*Gross:* (A.) Specimen consisted of two Fallopian tubes, each approximately 10 cm. in length. One tube showed a dilatation due to an intramural hemorrhagic mass at the point of junction of tube and uterus. The mass was 2 cm. in diameter. Definite decidual tissue could not be identified in this tube. The distal portion of the tube was not remarkable.

(B.) The other tube showed a hemorrhagic mass within the lumen at a point 3 cm. from the uterus. This hemorrhagic mass was more suggestive of decidual tissue.

*Microscopic:* Section through both Fallopian tubes showed islands of chorionic villi in the lumen surrounded by hemorrhage and decidual cells. The walls of the tubes were partially lined by decidual cells, and were thickened by a diffuse cellular infiltrate consisting of lymphocytes, plasma cells, and a few polys. The walls were moderately edematous.

*Diagnosis:* Bilateral tubal pregnancy.

*Delivery.*—Twenty-four hours after admission, the patient went into active labor and was medicated with 3 grains of nembutal and  $\frac{1}{100}$  grain of scopolamine. The latter was repeated in one hour. After eight hours of labor, the patient had a low forceps delivery under spinal anesthesia (70 mg. novocain). A median episiotomy was done. The blood loss was estimated to be 75 c.c. The infant was a 7 pound, 2 ounce boy, markedly asphyxiated. It gasped once and the cardiac impulse was palpable for twenty minutes. The usual methods of resuscitation failed and the infant succumbed. The umbilical cord was around the neck once, and it was observed that a loop had been caught in the left forcep blade. The infant appeared to be well developed. Autopsy examination revealed atelectasis.

*Postpartum.*—The patient's postpartum course was afebrile. A blood count taken one week after delivery showed: red blood cells 2,740,000; white blood cells 15,000; hemoglobin 48 per cent (7 Gm.). The blood Kahn was negative. A stool specimen was reported positive for *Endamoeba histolytica*, cysts of *E. coli*, ova of hookworm, ascaris lumbricoides, and *T. trichuria*. The patient was transferred immediately to the medical ward where therapy for helminths was instituted. One month later, she was discharged, free of "worms." A blood count at that time (Oct. 11, 1945) showed: red blood cells 3,900,000; hemoglobin 74 per cent (10.5 Gm.). The patient was asymptomatic, and a pelvic examination revealed normal involution of the uterus.

### Comment

It is interesting to note that the patient's complaints were relatively trivial compared with those one would expect from the clinical and laboratory findings. Our observations concerning ancylostomiasis astounded us in that the patients had very few subjective complaints. Most of them stated that they tired easily, experienced vertigo, and noticed some shortness of breath on exertion. Very few of them experienced syncope or extreme weakness. We concluded that the onset and progress of the anemia was so gradual that the patient adjusted himself to the condition, and was, therefore, able to live and work without much difficulty.

Dr. H. M. Zimmerman,<sup>1</sup> our pathologist, who performed the autopsies on many infants and children who succumbed to hookworm anemia, feels that the hookworm secretes an antigen which depresses the homopoietic centers, particularly the red-blood-cell-forming elements. Conversely, the white blood cells, especially the eosinophiles, are stimulated; consequently, most of the blood smears show an eosinophilia varying from 5 per cent to 33 per cent. Some writers<sup>2</sup> believe that the severe anemia is caused by the mechanical withdrawal of blood from the patient by the worms attached to the intestinal wall.

Some books on tropical medicine<sup>2, 3</sup> state that the red blood cell counts in patients infested with hookworm vary from one to three million, with hemoglobin readings varying from 20 to 40 per cent. This conclusion was verified in the thousands of Chamorros examined on Guam. The most severe anemias were found in infants, children, and pregnant women. Many patients in these groups had hemoglobin determinations of 2 to 4 grams. Despite multiple blood transfusions, many of the extremely morbid infants and children succumbed.

In almost every instance of edema associated with hookworm anemia, serum protein studies revealed evidence of hypoproteinemia. Investigators<sup>2, 3</sup> find that the plasma volume is increased, while the total blood volume is diminished. Blood cholesterol, serum proteins, and serum calcium determinations are low. These conditions are rectified simply by means of diet, calcium, blood transfusions, and serum albumin therapy.

was too thin. The patient was group B. The Rh determination was not done since anti-Rh testing serum was not available. The urine examination was essentially negative.

*Blood Transfusions.*—Shortly after admission, 1,300 c.c. of citrated, cross-matched, group O blood was given, without any reaction. This was followed with 200 c.c. of serum albumin. The blood count, 15 hours later, showed the hemoglobin to be 22 per cent; red blood cells 960,000; white blood cells 9,200; differential smear: neutrophils 79 per cent, lymphocytes 17 per cent, eosinophiles 4 per cent. The total proteins were 4.1 Gm. per 100 c.c. of blood. The presumptive Kahn was two plus.

The next day, eighteen hours after admission, the patient was given 1,000 c.c. of group O blood (uncross-matched) and 100 c.c. of serum albumin. Blood counts taken twenty-four hours later showed: hemoglobin 22 per cent (3.5 Gm.); red blood cells 1,020,000; white blood cells 11,200.

*Hospital Course.*—Besides blood transfusions, the patient was given 1 c.c. of liver extract intramuscularly, daily; ferrous sulfate grains X, three times a day; and multivitamin pills three times daily. She was placed on a high protein, salt-free diet.

The fluid intake during the first twenty-four hours was restricted to 1,000 c.c. by mouth. The output was not recorded, but the patient experienced marked diuresis following the serum albumin therapy, and, within forty-eight hours of admission, there was only a two-plus pitting edema. Absolute bed rest was maintained until the sixth hospital day when the patient was edema free. The total proteins on the eighth hospital day had risen to 5.8 Gm. per 100 c.c. of blood; red blood cells 3,170,000; hemoglobin 60 per cent; white blood cells 10,650; the differential smear revealed: neutrophils 83 per cent, lymphocytes 5 per cent, eosinophiles 11 per cent, basophiles 1 per cent.

The stool specimen showed many ova of hookworm. Since tetrachlorethylene was unavailable, oil of chenopodium was given in 15 minim doses, every thirty minutes, for three doses. A stool examination one week later showed ova for hookworm, ascaris lumbricoides, and the larvae of *S. stercoralis*.

On the sixteenth day, the patient was discharged from the hospital with a hemoglobin of 72 per cent (10.5 Gm.) and a red blood cell count of 3,420,000, and was referred to the prenatal clinic. Ferrous sulfate therapy was continued. The admission weight was not recorded. The discharge weight was 135 pounds.

*Prenatal Course.*—During the next three months, on a diet enriched with canned milk, eggs, and cheese, the weight gain was seven pounds. The patient was seen every two weeks in the prenatal clinic until the eighth month; thereafter, she was examined every week. Tetrachlorethylene (3 capsules) was given at the seventh month. Mapharsen and bismuth were administered for latent yaws. Repeated blood counts revealed a gradual increase in the red count and hemoglobin. On August 13, two and one-half months after the hospital admission, the red blood cell count was 3,550,000, the hemoglobin 83 per cent (12.0 Gm.).

*Labor.*—The patient was readmitted to the hospital on September 10, with premature rupture of the membranes. The blood picture at that time showed: red blood cells 3,870,000; hemoglobin 68 per cent (9.5 Gm.). Physical examination revealed the patient to be in excellent condition. The blood pressure was 110/80. There was no edema. The weight was 142 pounds. The uterus was almost term size, with the infant lying in the left occipitoanterior position, head partially engaged. The infant's weight was estimated to be 6 to 6½ pounds. Rectal examination revealed the cervix not effaced nor the os dilated. Liquor amnii definitely was escaping from the introitus.

# GAS BACILLUS INFECTION PRIMARY IN THE UNBORN FETUS, WITH REPORT OF A CASE SPONTANEOUSLY OCCURRING AT TERM, THE MOTHER SURVIVING

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(From the De Paul Hospital)

A NEGRO primipara (Case No. 17646), aged 23 years, was admitted to Maternity Center Clinic, July 6, 1943, in her third month of pregnancy. Her general health was excellent, she had had no abortions or operations, she showed no sign of vulval or cervical infection, smears were negative for gonorrhea, and the Wassermann was negative.

In January, her ninth month, she developed hypertension and albuminuria that increased notwithstanding home treatment so that on Jan. 20, 1944, she was sent to the hospital as a pre-eclamptic at term. Blood pressure was 170/115, and albumin was 2 plus. The fetal position was diagnosed as right occipitoposterior. Her nonprotein nitrogen was found to be only 28 milligrams.

After castor oil and an enema, pains began about 1 A.M., January 21. Two hours later, according to the nurses, the membranes appeared at the vulva and spontaneously ruptured. The patient was moved to the delivery room. After three hours, pains lessened and she was returned to her bed.

At 10 o'clock that morning, I found the head barely engaged, position right occipitoposterior, the fetal heart heard for what proved to be the last time, amniotic fluid draining away, the cervix only about 1 cm. by rectal examination with effacement estimated at 30 per cent, temperature normal, and blood pressure 170/90.

Through the rest of January 21 and 22, her labor was that of the usual occipitoposterior, with slow dilatation and ineffectual pains. Four per cent mercurochrome was instilled into the vagina four times, beginning at 9 P.M. on January 21. This was the only invasion of the vagina before delivery.

On January 22, the pelvis was confirmed as adequate by x-ray. That evening, her temperature rose to 100° F., but it was thought to represent only the stress of labor and dehydration. There was no other rise before delivery.

At 2:30 A.M., January 23, dilatation was complete and the head was bulging the perineum. Up to this time, no abnormality of the fetus, other than simple death, was suspected. At 3:30 A.M., the caput was in sight, and, much to our surprise, felt like a bag of water. No bone was palpable.

Believing it to be hydrocephalus, the scalp was clipped with scissors; necrotic brain tissue and gas burst forth under pressure, with an odor far more foul than *bacillus coli*. The contents of the cranial vault was completely liquefied. Though the bones of the vault were not palpable at this time, the pathologist later reported that the centers were still present.

Birth was accomplished without apparent damage to the maternal soft parts, other than an episiotomy.

The condition of the placenta was carefully noted, but, macroscopically, it showed no pathology. It was not sectioned.

The child's development appeared normal, and weight was estimated at 7 pounds. There was marked gaseous distention of the abdomen, and subcutaneous crepitation was definite in all limbs. The skin was discolored but not macerated.

The autopsy, by Dr. Arnold F. Straus, pathologist, showed: "Skin throughout grayish red with greenish discolorations, but not macerated. General subcutaneous crepitation, and evil odor. On opening, muscle tissue shows gas blisters. The pleural, pericardial, and peritoneal cavities, all show a small amount of hemorrhagic fluid. All organs showed a

During a two-year period (1932-1933), at the De Soysa Lying-in Home, Colombo, Ceylon, Wickramasuriya,<sup>4</sup> in a study of hookworm disease as a complication of pregnancy, reports a maternal and infant death rate of 27 per cent and 23 per cent, respectively. He states that ancylostomiasis was, by far, a greater menace to the expectant mother and unborn child than were puerperal sepsis, eclampsia, pyelitis, and postpartum hemorrhage. The majority of the sufferers of severe hookworm anemia succumbed to cardiac failure either during or after delivery. He further relates that abortions, miscarriages, and stillbirths were very commonplace. Furthermore, many young women were rendered unfit for motherhood either as a result of cardiac disability or defective renal function, or both. Evidently, many of the deaths reported were in unregistered patients who were admitted to the hospital in extremis. Since no mention is made of blood transfusion therapy, one would expect a high maternal death rate. The Chamorros on Guam were urged to register for prenatal care early in pregnancy; the severe cases of hookworm anemia were immediately hospitalized and given multiple blood transfusions. As a result of prenatal care, not a single mother succumbed in the 838 patients delivered during the interim of Dec. 1, 1944, to Dec. 1, 1945. It was noted in the early days of establishing the clinics that the incidence of abortions, miscarriages, and stillbirths was high. However, as a result of the commendable cooperation of the expectant mothers in attendance of the clinics, the gross fetal mortality rate for the year was only 5 per cent.

In the early days of the prenatal clinics, a survey of the stool examinations revealed that 95 per cent of the patients were infested with intestinal parasites, particularly hookworm and *ascaris lumbricoides*. At the end of one year, 73 per cent of the undelivered patients showed worm infestation. A survey of the treated delivered patients was not completed. Prior to the American invasion in July, 1944, helminthogogues had never been administered to pregnant women on Guam. They feared that the "worm medicine" would affect the unborn child or cause abortion. After prenatal clinics, twelve in all, were established over the island, every patient who had a positive stool was treated. Not a single patient aborted, miscarried, or delivered prematurely. Most of them averred that they felt much better. Certainly, the infants delivered from the treated group were healthier, and the likelihood of helminthiasis was reduced.

A question arose as to whether or not the hookworm larvae passed from the maternal circulation to the fetus. Therefore, the meconium was examined in a large number of newborn infants, with the result that all stools were negative for any type of parasite. The infants were infected shortly after birth because of unsanitary living conditions.

Without any doubt, the incidence of worm infestation was markedly increased during the Japanese occupation, since little or no medical attention was given the people of Guam, and they were forced to live under unspeakably filthy conditions. Several years of enforced public health principles will eliminate the extensive prevalence of parasitic infestation which still exists.

The views and statements in this communication are not necessarily accepted and confirmed by the U. S. Navy.

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## Discussion

Authors seem to have agreed that devitalized tissue is fundamentally necessary for the *Clostridium welchii* to implant itself and propagate in sufficient numbers to initiate active infection.

May it not be that amniotic fluid is a satisfactory culture medium, and the particular medium that carries infection into the uterine cavity, in the absence of instrumentation and trauma? There seems to be very little written about amniotic fluid as a culture medium. If true, it would explain much about abortion and prenatal infections. Cosgrove and Barry discuss at some length the exact manner in which the gas bacillus, dormant in the cervix, may become active and reach the fetus, when there is no dead tissue present. In their case, as apparently in all others of this type, the membranes ruptured early. Progress of the infection upstream into the amniotic sac is probably aided by the contractions and relaxations of the uterus in labor.

What caused the baby's death, in our case? Was it maternal toxemia, interference with circulation in the cord, or the infection? Had the circulation ceased before it was attacked by gas organisms, or did gas bacilli attack a living baby?

In treatment, how much benefit was derived from the simple admission of air into the vagina twice daily for six days, when the sulfanilamide powder was introduced? This was admitting air to the focus of an anaerobic organism. Is this treatment entitled to particular credit?

## Summary

1. The rarity of gas bacillus infection that is primary in the unborn fetus is noted.
2. A case of such infection following premature rupture of membranes at term is reported.
3. This fetus showed liquefaction of the brain and generalized gas infection, which had developed without giving symptoms in the mother.
4. The trauma of delivery promptly started active infection in the mother; life was threatened for seven days, followed by recovery.
5. Treatment consisted only of (1) serum, a prophylactic dose on the first day, and a therapeutic dose intravenously on the second; (2) sulfanilamide and soda by mouth, for seven days, but only to a blood concentration of 5 mg.; (3) sulfanilamide powder into vaginal vault, through a bivalve speculum, twice daily; and (4) supportive treatment of intravenous glucose.
6. Though the virulence of the strain probably was not maximum, recovery was unexpected.
7. The possible role of amniotic fluid as a culture medium that initiates the growth and spread of the infection in the absence of dead tissue is suggested.

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dirty grayish red, discolored and cloudy. Direct smears from blood and liver were loaded with gram-positive rod-shapes. Cultures from blood and liver showed gas-forming and spore-forming gram-positive bacilli in buffered medium."

Four hours after delivery, the mother's temperature was 104.6° F. A therapeutic dose of gas serum was ordered, but, through misunderstanding, a prophylactic dose of 1,500 units was all she received that day.

The next day, January 24, her temperature continued near 104° F., but she had no chill. Hemoglobin was reported 103 per cent, and red blood cells 5,100,000. A therapeutic dose of serum—*Cl. perfringens* 10,000 units and *Vibrion septique* 10,000 units—was given intravenously. Sulfanilamide, initial dose 3 grams with sodium bicarbonate, and 1 gram every four hours, was started. Penicillin was not then available.

On January 25, her second day, hemoglobin was 94 per cent, red blood cells 4,620,000, white blood cells 13,400, and polys 71 per cent. Through a bivalve speculum, a culture was taken from the cervix, after which 5 grams of sulfanilamide powder were placed in the vaginal vault. This treatment was continued twice daily.

Consultation with an obstetrician and a surgeon was obtained. They considered the case hopeless, and offered no suggestions as to treatment.

A blood culture taken on January 26 was negative.

During the first two days post partum, the patient had mild vomiting; during the third and fourth days, she had loose stools. The abdomen was moderately distended and tender. Intravenous glucose, 1,000 c.c. of 10 per cent, was given.

Her temperature remained between 102° and 104.6° F. for five days. It reached normal on the seventh day, and there was no further rise.

The episiotomy wound opened completely and was covered with a thick dirty-gray slough. Sulfanilamide powder cleared it promptly, and the wound healed by granulation.

Blood sulfanilamide reached its peak on January 27, 5 mg. per 100 c.c. On January 30 it was 4 mg.

The culture taken from the cervix on January 25 showed gram-positive gas-forming rods and capsules, hemolytic and nonhemolytic streptococci, *B. coli*, and *Staphylococcus albus*.

We were amazed to see this patient begin to improve. Treatment had not been strenuous, nor very prompt. However, she was discharged from the hospital February 5, her thirteenth day, comfortable, eating well, with blood pressure 130/80, fundus 4 cm. above the symphysis, and lochia scant and colorless.

One month later, at the clinic, she appeared in perfect health, the pelvis showed no inflammatory residue, and she was discharged.

Incidentally, she again became pregnant in three months. She carried to term and had a normal spontaneous delivery at home, under clinic supervision, in January, 1945. There was no morbidity this time.

Our theory regarding this case is that gas bacilli were carried into the vagina by sexual intercourse, which admittedly occurred as late as two days prior to admission to hospital. In the cervix, spores remained dormant until membranes ruptured forty-eight hours before delivery. Then, by some route, probably amniotic fluid, nostrils, and cribiform plate, they reached the meninges and brain of the baby. Brain tissue, more particularly dead brain tissue, being the best-known culture medium for the gas bacillus, there was time for the organism to flare into virulent activity and produce the pathology found. Also, some of the infected amniotic fluid may have been inhaled and ingested, infecting lungs and intestinal tract. The mother's tissues were not attacked before delivery, because up to that time she had no devitalized tissue. The placenta, too, appeared to be an effective barrier, for the mother's protection.

We were fortunate, here, in the comparative absence of mixed infection. As pointed out by Dyke, the mixed infection probably multiplies the trauma and adds to the liberation.



skull of a breech presentation through a thin abdomen.<sup>2</sup> This finding, when elicited, may be of positive assistance in the diagnosis of a breech presentation.

It was observed that if the presenting pole was steadied over the inlet by impressing the fundus from above by the external hand of the examiner, and the presenting pole explored through the lower uterine segment, the sensation of buckling, as if a derby hat were compressed, was felt if a vertex presented. This was noted through lower uterine segments that were thick, as well as through those that were thin. The palpatory sensation is similar to that described in the cephalic palpation of the rachitic skull with craniotabes.<sup>6</sup> The presence of this sensation indicates a vertex presentation. While this does not offer a positive assistance in the diagnosis of breech presentation, in a negative way, it has helped rule out the possibility of breech in numerous equivocal cases when x-ray was not immediately available and vaginal examination was not desirable.

It has been found that not all presenting vertices will give this sensation, but a great many will. One must be cognizant of the urgency for gentleness in the rectal exploration so that the buckling that is felt is a finding in the palpation rather than the result of denting of the fetal skull from a vigorous probing of the presenting fetal pole. The finding is offered merely as an adjuvant in the diagnosis of fetal polarity.

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## AN AID IN THE DIAGNOSIS OF FETAL POLARITY

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**A**N ACCURATE clinical diagnosis of the fetal polarity in the obstetric patient in labor is most important. Abdominal findings (position of the fetal heart, palpation of the fetal small parts, palpation of the upper and/or lower pole of the fetal axis) are often inconclusive because of: (1) the obesity of the patient, (2) the voluntary resistance and uncooperative posture, (3) the inferential character of the findings.

The patient in labor with a breech presentation offers a problem separate and apart from the same patient with the identical fetus presenting as a vertex. The greater efficiency of the vertex as a dilating pole is universally known and accepted. The vertex presentation with slight or moderate cephalopelvic disproportion often resolves itself following adequate labor, with molding of the head, and vaginal delivery is accomplished without great difficulty. The same head coming through the pelvis as the aftercoming head of a breech presentation offers an entirely different problem. No opportunity is afforded the head to become molded and accommodate to the pelvic configuration. As a result of the dystocia and the frequently difficult vaginal delivery, a disastrous result may be the eventuality to the baby and, at times, to the mother. The fetal mortality in breech presentation averages about 14.1 per cent (Hirst 20 per cent,<sup>1</sup> Curtis 13 per cent,<sup>1</sup> Williams 10-14 per cent,<sup>1</sup> Stander 13.1 per cent,<sup>2</sup> Beck 10 per cent,<sup>3</sup> DeLee-Greenhill 6-32 per cent,<sup>4</sup> Margaret Hague 11.2 per cent.<sup>5</sup> While the maternal mortality in breech presentation is not significantly different than with vertex presentation,<sup>2, 4</sup> the incidence and severity of perineal and soft tissue injury is materially greater.<sup>1, 2</sup>

Mindful of the necessity of making the clinical diagnosis of breech presentation more accurate and precise, the writer attempted to find some additional information that would be of assistance. No positive findings to assist in the diagnosis of breech presentation could be determined other than the well-known findings of: palpable vertex in the uterine fundus, fetal heart tones in one of the upper abdominal quadrants, absence of cephalic prominence over the symphysis, and palpation of a soft, compressible breech, rectally or vaginally.

These findings are adequate in the patient whose abdominal wall and voluntary posture permit satisfactory palpatory examination and whose cervix is sufficiently effaced and dilated to permit thorough palpation and exploration of the presenting pole, rectally. It was found, however, that upon rectal examination the presence of a thick lower uterine segment with an uneffaced, undilated cervix offered a rather difficult medium through which to confirm the presence of a breech or vertex over the pelvic inlet.

Stander has mentioned a "characteristic crackling sensation upon compressing the bones of the skull" obtained occasionally upon palpation of the

unusual. Disappearance of polyuria and polydipsia during pregnancy and their return afterward are not unusual features. The persistence of nausea and vomiting and the development of pre-eclampsia in the presence of this syndrome would suggest that copious fluids are not always adequate treatment for these complications of pregnancy. The simultaneous regression of diabetes insipidus and onset of pre-eclampsia might lend support to the antidiuretic theory of this toxemia. On the other hand, since the diuresis was never completely overcome, we might assume that pre-eclampsia is the cause rather than the result of the antidiuresis. The immaturity at term of an otherwise normal infant is interesting.

## DIABETES INSIPIDUS AND PRE-ECLAMPSIA

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THE following case is reported because it deals with a patient with long-standing diabetes insipidus, who became pregnant and developed a severe pre-eclampsia. With progression of the pre-eclampsia, the polyuria and polydipsia almost disappeared, only to recur gradually after delivery.

This patient, white, 27 years old, was first seen Nov. 25, 1944, with the usual presumptive signs of pregnancy. Her last period was July 20, 1944, which made her confinement date April 27, 1945. Her menarche occurred at 14 years of age, followed by scant, painful, three-day periods every thirty days.

Her past history is significant only as it related a tremendous thirst and comparable urinary output for over twenty years' duration. She placed her intake of fluids at as much as eight gallons in twenty-four hours. She urinated often—hourly during the night. A transfusion reaction when five years old was supposed to have been responsible for this condition. Due to previous experiences, she requested that her diabetes insipidus not be treated.

Physical examination was negative except the pelvis. The bladder was distended and the uterus was enlarged and gravid. Genitals were nulliparous. Generally she appeared healthy and well nourished. Her blood pressure was recorded at 120/75, and her weight was 121½ pounds. Serology was negative, her red blood count was 2.6 million, and hemoglobin 61 per cent, urine specific gravity was 1.004.

Her prenatal record shows an unusual persistence of nausea with some vomiting and increased nervousness and sleeplessness. In January, the sixth month, her blood pressure became elevated and varied between 140/90 and 185/115 until delivery. In February, the seventh month, water intake and output diminished greatly, and sweating became profuse day and night. Albumin was detectable from early March until delivery. A coincidental left facial paralysis developed in March also and gradually improved after several months. On March 16 she was hospitalized for control of the pre-eclampsia. According to hospital records, her intake and output (specific gravity 1.004) reached a new low in her memory of about one gallon in twenty-four hours. Because her fetus was quite small, she was dismissed five days later without induction of labor.

On April 16 the patient was again hospitalized because of severe pre-eclampsia. Prior to delivery her intake approached normalcy (about 1,500 c.c.), while the urinary output (specific gravity, 1.010) usually exceeded this by nearly 1,000 c.c. This discrepancy occurred in spite of the absence of clinical edema. On April 25 labor was induced medically, and after five hours of labor a 4½-pound immature baby was delivered spontaneously and lived. The postpartum course was uneventful except for slight morbidity. On the third postpartum day intake and output again exceeded one gallon each. By August, four months post partum, her intake and output (specific gravity, 1.004) exceeded two gallons daily. Her blood pressure has been normal since her examination six weeks after delivery.

This case of diabetes insipidus and pregnancy provokes some interesting conjectures. The development of a severe pre-eclampsia makes this case more

2. The patient then assumes an erect position on a low stand situated at the examiner's end of the examining table, turns about face, places the knees on the edge of the table and assumes the knee-chest position.

3. Re-examination allows the vagina to expand with air. Downward pressure is made on the lateral bars of the pessary, alternating with backward pressure on the cervix, while the patient coughs several times. These measures usually produce anteroversion of the uterus (Fig. 1, *C*).

4. The patient falls slowly into the prone position momentarily and then rolls over into the original lithotomy position.

5. Re-examination and any further manipulation for completion of the uterine replacement is carried out per vaginam (Fig. 1, *D, E*).

6. Routine instructions as to douches and revisits are given.

Fifty-five patients with retroversion uteri in early pregnancy, or not pregnant have been treated with the above technique. No failures have occurred, probably because no fixed retroversions have been encountered. One patient had an incarcerated uterus with a three and one-half month gestation which resisted the usual method of replacement since manipulation was painful. She was suffering from severe sinusitis which was a contraindication for replacement under general anesthesia. The combined technique gave an excellent result, with complete relief of symptoms. It is estimated that anesthesia was avoided in 10 patients with retroversion by employing the combined technique.

### Summary

1. A combined procedure is described for replacement of the retroverted uterus based on the preliminary insertion of a well-fitting pessary in lithotomy position which keeps the uterus from falling back after it has been replaced in the knee-chest position. The use of a tenaculum in replacement is unnecessary, and is often undesirable, especially in pregnancy.

2. The procedure has given good results in 55 cases. It was estimated that 10 cases would have required replacement under general anesthesia, which was obviated by the use of the combined technique. One patient had an incarcerated uterus with a three and one-half months' gestation that was readily replaced.

## COMBINED PROCEDURE FOR ANTEROVERSION OF RETROVERTED UTERI

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**R**EPLACEMENT of the retroverted uterus is not always possible when bimanual manipulation is performed in the lithotomy position. Attachment of a tenaculum to the cervix facilitates replacement in certain cases, but its use is undesirable for pregnant uteri. Correction in the knee-chest position may also be impossible, or if it is accomplished, the uterus falls back when the patient is subsequently re-examined for insertion of the pessary in the lithotomy position. Under such circumstances further attempts are either given up entirely, or replacement is accomplished under general anesthesia. The importance of the correction of malpositions of the uterus is beyond the scope of this article, yet the improved chances of conception, prevention of spontaneous miscarriage, relief of nausea in pregnancy, alleviation of backache, and treatment of the incarcerated pregnant uterus are acceptable indications. The contraindications are: absence of symptoms in nonpregnant women, vaginitis, and medical indication for a contraceptive diaphragm.

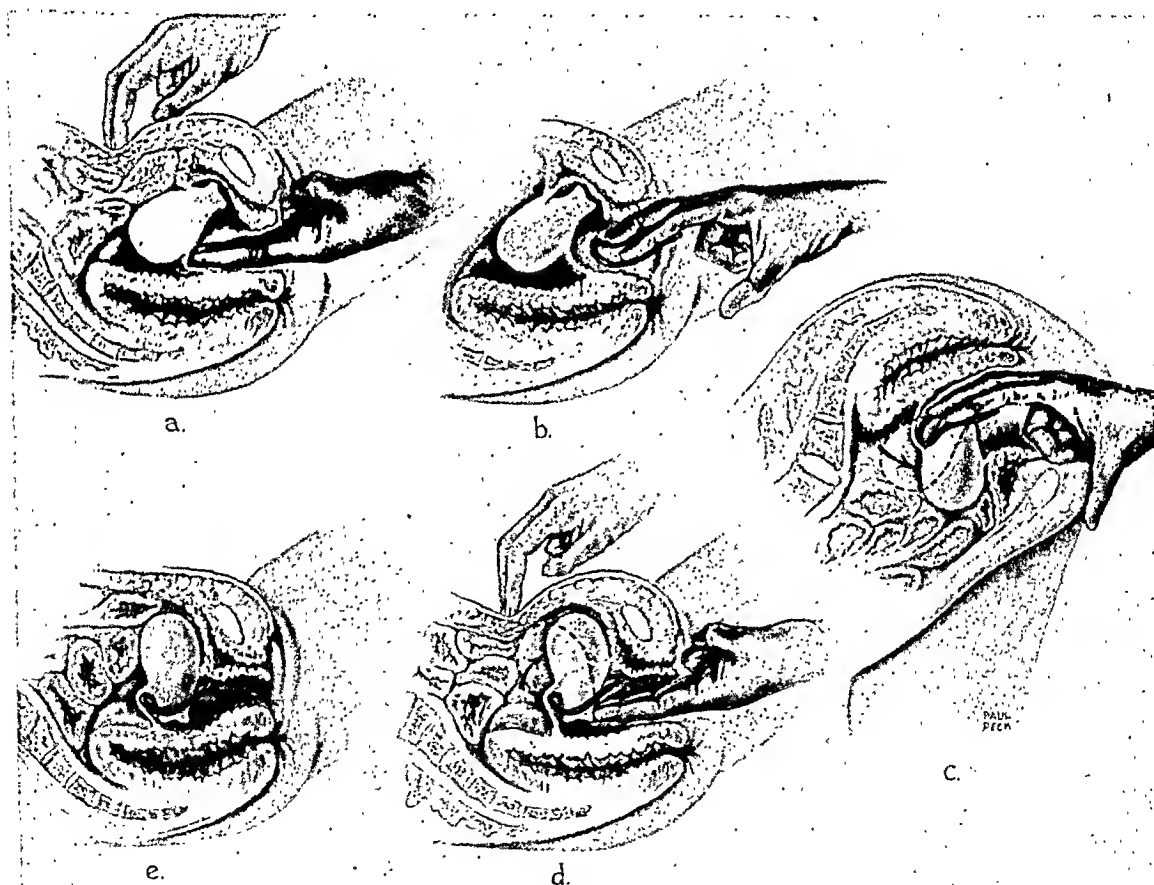


Fig. 1.—Technique of the combined procedure for manual replacement of a pregnant retroverted uterus.

The following technique has given uniformly excellent results at the Army Air Forces Regional Hospital at March Field, California:

1. The diagnosis of retroversion uteri having been made vaginally in the lithotomy position and the indications for replacement having been fulfilled; a well-fitting Smith-Hodge pessary is inserted (Fig. 1, A, B).

sired level by a thumbserew (3). On the horizontal member of the rod there are two movable sleeves (5), each of which is welded to two other sleeves at right angles, and through these pass the heavy tubing to the mask. The tube connections to the machine (6) have been inverted so they now point up instead of down, and right angle elbows (7) have been added to the mask so that it normally remains in proper relationship to the face.

Friction and tension cause the mask to remain at whatever level it is set, and this enables one to use the machine for continuous oxygen by simply moving the baby's head against the side of the crib and holding it there with a small sandbag, and then setting the machine on inhalation and adjusting the mask to the baby's face.

The modification is inexpensive and can be made by almost any mechanic. The connections at (6) were found to be soldered in and had to be heated in order to invert them.

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## MODIFICATION OF THE ERICSON AND JOHNSON RESUSCITATOR

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THE following modification of the widely used Ericson and Johnson resuscitator was devised with the idea of facilitating its use. Frequently one gets the impression, when using certain devices, that the designer had not actually used the device under normal operating conditions. In the case of the Ericson and Johnson resuscitator, we found that the relation of the tubing to the machine and to the mask made it needlessly difficult to hold the mask snugly and

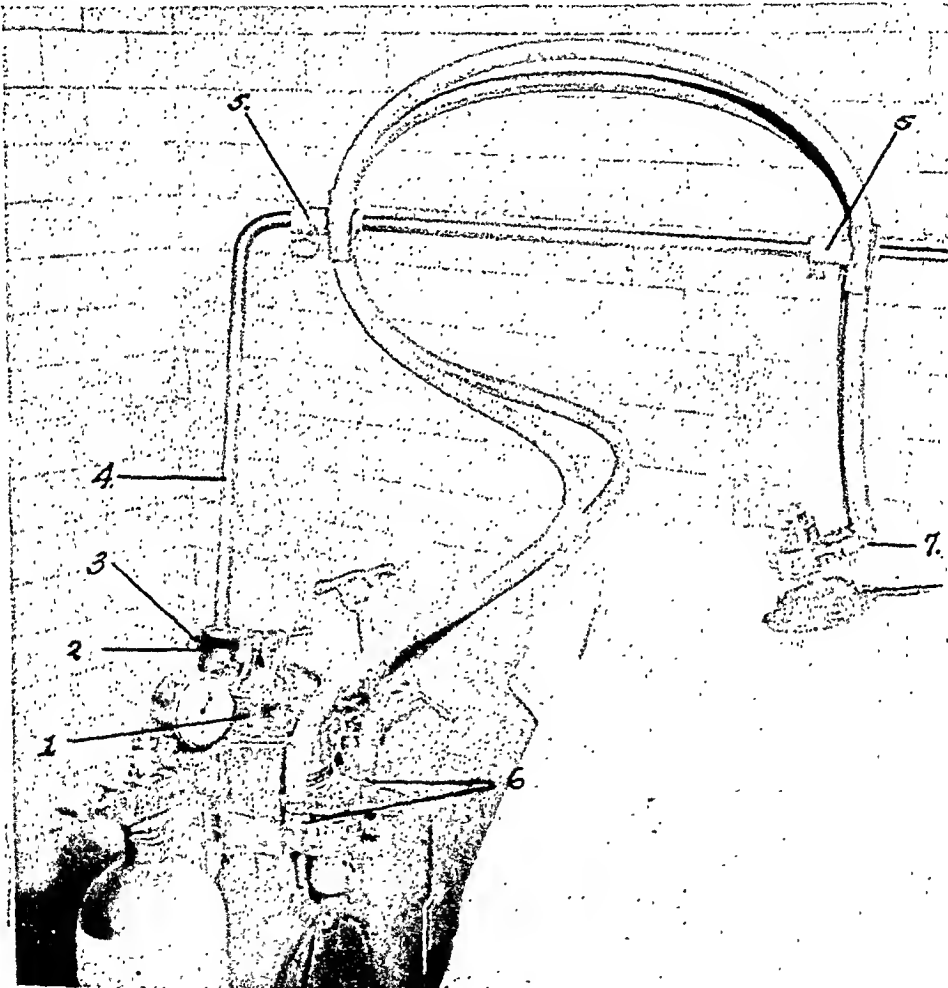


Fig. 1.

comfortably against the infant's face; and we also found a tendency, because of the weight and stiffness of the tubing, for the mask and tubing to fall to the floor whenever it was laid aside temporarily. It was with these problems in mind that this modification was developed.

Fig. 1 is to a large extent self-explanatory. A collar (1) was made to slip over the machine and fasten with thumb screws. Welded to this collar is a sleeve (2) through which passes an L shaped rod (4), which can be held at any de



The transmission from the low to the high temperature phase coincides with the ovulatory phase. The occurrence of this shift does not constitute a proof of actual ovulation. The use of the temperature record in the timing of intercourse and for other proceptive purposes is described. The waking temperature may also be employed in determining the postovulatory period during which conception will not take place.

CARL P. HUBER.

Mateos Fournier, Manuel: Artificial Insemination, *Prensa méd. mex.* 10: 13, 1945.

The author discusses the possible causes of sterility in the two partners of a childless union. If artificial insemination is found advisable, it is necessary first to fix the probable date of ovulation, which is fourteen days before the next menstruation in the woman with regular cycles. In the irregular woman, the minimal and maximal cycles are observed for a few months, the fourteen days subtracted, and the average is used, giving two or three monthly inseminations on the probable dates. The survival of the ovum is about twelve hours, and it is therefore difficult to obtain a satisfactory result from insemination; hence the procedure has to be repeated several times.

Simultaneously, the woman is submitted to a treatment of stimulating ovulation by means of extracts of the anterior lobe of the hypophysis, and the husband is advised not to have intercourse for several days preceding the insemination. In some cases he is also given hormonal extracts to stimulate maturation of his sexual elements.

The semen must be obtained by masturbation and deposited in a dry, sterilized glass container, such as a Petri dish which is then floated in a tray with some tepid water. When it is absolutely impossible to collect semen in this way, it is taken from the vagina immediately after coitus. In cases of oligospermia, the semen is centrifuged and the precipitate used. Insemination offers no difficulties, and the site selected for it may be vaginal, cervical, uterine, or tubal, depending on the findings of the case. In intrauterine maneuvers, the greatest care must be taken to avoid bleeding and contractions which may expel the semen. For the same reason, only one or two drops of the fluid are introduced. Sometimes, especially in sensitive women, antispasmodic medication is administered before and after the maneuver. A short rest on the operating table and bed rest for several hours at home are recommended. Over-all success of from 25 to 30 per cent can be expected.

J. P. GREENHILL.

## Gynecology

Kovacs, F.: The Significance, Diagnosis, and Treatment of Female Genital Tuberculosis, *Monatschr. f. Geburtsh. u. Gynäk.* 116: 183, 1943.

The author encountered 191 cases of tuberculosis of the female genitalia in his private practice. Hence this disease is much more common than is generally appreciated. In 60 per cent of the cases, sterility is present. The most important diagnostic procedure is curettement and examination of the endometrium. In 60 per cent of the cases of genital tuberculosis, the uterine scrapings will reveal the disease. Hence this diagnostic measure should be used more widely. Likewise, curettement should be performed in all cases of sterility and menstrual disturbance. A careful curettement entails no danger of spreading the disease.

The conservative treatment of genital tuberculosis has not proved effective. Hence the author recommends early laparotomy as the best treatment. This form of therapy quickly eliminates the source of infection. In early cases, the ovaries need not be removed. Removal of the uterus is not a sacrifice, because these women are sterile anyway. The presence of pulmonary tuberculosis is not a contraindication to operation.

J. P. GREENHILL.

Hodgson, J. E., Dockerty, M. B., and Mussey, R. D.: Granulosa-Cell Tumor of the Ovary, *Surg., Gynec. & Obst.* 81: 631, 1945.

The authors present 62 instances of granulosa-cell tumor occurring in the Mayo Clinic from 1910 to 1944. This comprises 1.63 per cent of 3,800 ovarian tumors seen during that

# Department of Reviews and Abstracts

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## Selected Abstracts

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### Sterility, Fertility, Contraception

Halliday, J. L.: Psychosomatic Medicine and the Declining Birth-Rate, *Lancet* 248: 601, 1945.

Halliday's purpose of his article was to suggest the value of applying a psychological approach to the problem of declining birth rate.

The author insists that behavioral sterility, increasing frequency of practice of birth control, usually by coitus interruptus, is an expression of neurotic anxiety. This induced sterility could often be related to the obsessional characteristics, in that, persons with such a rigid character structure tended to experience upsetting events, as childbirth and children, as a threat to the routine but precarious design for living in a dangerous and disturbing war period:

The writer is of the opinion that birth rate represents a sound index of psychological health. Between 1870 and the recent war periods, mass unemployment, financial crisis, increasing competition, decline of active religious faith, a desire for personal safety, and a preponderance of other as unfavorable factors occasioned an increasing social disintegration provocative of a declining birth rate. If the fertility rate (England and Wales) of 1870 were to be considered as 100 per cent, the drop in fertility by 1900 (the mildly anxious generation) was 25 per cent, and the drop by 1930 (the second and definitely anxious generation) was 59 per cent.

Halliday illustrates his suggestions for therapeutic standards in the national attempt to alleviate parental anxiety—that every mother receive for each child in its early formative years (up to the age of 3 or 5 years) everything that is required—food, clothes, perambulators, go-carts, baby chairs, utensils—everything—without charge and irrespective of social class. This positive step would relieve parental anxiety and provide a sense of belonging to the community.

If added nursery facilities were available *and used*, the present generating neurotic parents would be relieved of further tensional loads.

Other examples of therapeutic measures to treat social disintegration include the choice of scientific selection for pupils in schools in contrast to aggressive competition; vocational guidance; compulsory labor camps or their equivalent; and "social security" in its psychological sense—i.e., security against preventable neurotic anxiety.

Halliday concludes that only such therapeutic measures as are based on understanding of the primary etiological relevance of psychosocial factors can help to provide a generation of young persons less inhibited by neurotic anxiety and, as a consequence, socially more healthy, psychosomatically less incapacitated, and biologically more fertile. C. E. FOLSOME.

Barton, Mary, and Wiesner, B. P.: Waking Temperature in Relation to Female Fecundity, *Lancet* 11: 663, Nov. 24, 1945.

In fecund women the body temperature on waking in the morning varies with the phases of the menstrual cycle. A relatively high temperature is characteristic of the premenstrual phase and it persists after conception. Persistent low temperature excludes the diagnosis of pregnancy. The diphasic temperature cycle may persist in cases of amenorrhea, but more commonly amenorrhea is characterized by a monophasic waking temperature record. Certain types of infecundity are associated with absence of the high temperature phases.

in dealing with women patients increased, minor operative procedures, such as curettage or dilatation (for dysmenorrhea) became increasingly unnecessary. The gap between the practicing physician and the psychiatrist must be bridged, but, in the author's opinion, this can best be done by enlarging the sphere of the practitioner. The family physician has the advantage of close contact with the patient and firsthand knowledge of family peculiarities and tendencies. He also sees the patient early enough, in the curable stage, before the family reactions have become fixed and irreversible, but, to effect a cure in this stage, he must have "the requisite interest and knowledge."

Schaub, Isabelle G., and Davis, James E.: The Significance of Streptococci Isolated From the Female Urinary Tract, Bull. Johns Hopkins Hosp. 77: 372, 1945.

The authors summarize the article as follows:

The histories of 500 patients from whose urine specimens streptococci were isolated have been carefully studied from a clinical standpoint, and conclusions reached in regard to the significance of the organisms.

Streptococci were found to be the sole cause of clinical disease in 25.2 per cent of the cases reviewed, and involved with other organisms in 28.8 per cent. In a total of 54 per cent of the cases, therefore, they were regarded as etiologically significant. In 6 per cent of the clinical cases studied, the role of the streptococcus was doubtful.

In 40 per cent of the patients from whose urine streptococci were isolated, no clinical evidence of urinary tract disease could be found in the history. The significance of the presence of streptococci in this high percentage of cases is discussed.

The relative occurrence of the various streptococci with *Escherichia coli* was studied and it was determined that the alpha and gamma enterococci were involved with *E. coli* in a significantly higher percentage of cases than the other streptococci with the exception of the gamma streptococci.

C. O. MALAND.

Hardy, Harriet L.: The Clinical Significance of Data Accumulated in the Medical Care of Young Women, New England J. Med. 233: 811, 1945.

One of the purposes of this paper is to point out the wide range of physiologic variations that are possible among normal young women. The blood pressure readings in 1,000 college women between the ages of 16 and 22 years are recorded. Seldom, if ever, is it found that a low blood pressure reading and fatigue are directly related. A study of the white blood cell counts in the menstrual cycle revealed that for practical purposes of differential diagnosis, there was found in this study no suggestion that the white cell count undergoes a physiologic shift at any time in the menstrual cycle.

From this study it is concluded that since red cell counts and hemoglobin levels slightly lower than normal are apparently not related to fatigue, menstruation or infection, and produce no other symptoms, the body is able to manage efficiently with what has been considered to be less than the normal blood level. The author advises treatment, however, for an iron deficiency.

JAMES P. MARR.

### Labor, Management, Complications

Bret, J., and Deplus, J.: Obstetrical Consequences of Uterine X-ray Therapy. Frequency of Abortion and Cervical Dystocia, La Presse médicale 53: 255, 1945.

The authors studied the effects of radium therapy on subsequent pregnancies and labors. Regardless of the dose of radium used it produces sclerosis, particularly of the cervix. Because of this sclerosis, operative interference at the time of labor is necessary in 60 to 70 per cent of women who conceive after radium treatment. Furthermore, the sclerosis which also affects the uterine endometrium may result in disaster. Among 34 pregnancies in 23 women who became pregnant after irradiation, there were nine abortions and six premature labors. The 34 pregnancies yielded only 12 living children (36 per cent). The fetal deaths were by



Symptoms of vomiting, abdominal pain, edema, and purpura, together with fever and leucocytosis were manifest in the first case. Vomiting, dyspnea, pallor, and leucocytosis characterized the clinical picture of the second case. In both instances the disease ran a fulminating course, and the diagnosis was not suspected before autopsy. C. O. MALAND.

**Albaugh, C. H.: Congenital Anomalies Following Maternal Rubella in Early Weeks of Pregnancy, J. A. M. A. 129: 719, 1945.**

Nine cases of congenital abnormality in the infant following an exanthem in the mother in the early weeks of pregnancy are herewith reported. The pathologic lesions associated with rubella are reviewed. The importance of this problem from a public health point is stressed. Various public health measures for control are enumerated. The most common lesions in infants born of mothers who contracted rubella during pregnancy are cataracts, cardiac septal defects, patent ductus arteriosus, deaf mutism, and microcephaly. Nearly all of the infants are poorly developed and present a feeding problem. WILLIAM BERMAN.

**Kendig, Edwin J., Jr., and Fiske, Russel H.: Penicillin Ointment in the Treatment of Impetigo Neonatorum, J. A. M. A. 129: 1094, 1945.**

In 14 cases in which penicillin ointment had been used there were no new lesions after the treatment had been in effect for forty-eight hours. After a maximum of three days all the lesions appeared to be dry and healed. In three instances, however, there was a recurrence of the condition after the patient had been home from the hospital more than one week. Each recurrence was after treatment had been discontinued and baths had been started.

WILLIAM BERMAN

**Bloxson, Allan: Penicillin Locally in the Eyes of Newborn Infants to Prevent Ophthalmia Neonatorum, J. Pediat. 27: 447, 1945.**

An additional case of gonorrheal ophthalmia neonatorum developed after the use of a silver preparation in the Credé method of prevention. Four drops (250 units per cubic centimeter) of penicillin was instilled in each eye every four hours. This occurred in a nursery of twenty infants having been exposed to a possible gonorrheal conjunctivitis, and resulted in no further spread of the infection in the nursery.

The result suggests that penicillin locally can and should be used as a specific prophylactic agent in the Credé method of prevention of ophthalmia neonatorum.

JAMES P. MARR.

**Harris, Evelyn S., and Platou, Erlin S.: Pyopneumothorax in a Premature Baby Successfully Treated With Penicillin, Am. J. Dis. Child. 70: 226, 1945.**

The authors report a case of pyopneumothorax seen in a premature infant seven days after its onset. It appeared that sulfamerazine was failing to influence the course of the disease. Penicillin was given over a period of fifteen days.

The possibility and early recognition of pulmonary infection following atelectasis in premature infants should be emphasized.

JAMES P. MARR.

**Freud, Paul, Rhodes, Adrian W., and Weisz, Albert: Hereditary Skin Defect in the Newborn Infant, J. Pediat. 27: 591, 1945.**

The authors report an interesting case of hereditary skin defect of the scalp in a newborn. For the first time, the same defect in the same location was also found in the parent.

JAMES P. MARR.

no means all due to operative intervention. Some of them were born dead or were macerated. There were no fetal malformations in this group.

In the women who continue to term, premature rupture of the membranes is almost the rule. The membranes and placenta may adhere to the decidua in the lower uterine segment. In 50 per cent there are disturbances in the contractions of the uterus. Cervical dilatation reaches a certain point and then stops. These occurrences along with fetal death often lead to amniotic infection which is usually serious. In many cases the cervix must be incised and forceps used, often with disastrous results for mother and baby. In some cases embryotomy must be performed. Sometimes even this is impossible, and the entire uterus must be removed in one piece.

J. P. GREENHILL.

Chanal, G.: Different Methods of Inducing Labor. The Medical Method and Its Results at the Geneva Maternity, *Monatschr. f. Geburtsh. u. Gynäk.* 119: 69, 1945.

At the Geneva Maternity, Stein's medicinal method of inducing labor is used. The procedure carried out is as follows: the patient is given 60 Gm. of castor oil in one dose, 1 Gm. of quinine sulfate given four times at half-hour intervals, and 10 Voegtlin units of thymophysin, given three times at half-hour intervals. If labor pains are inadequate, three drops of Basergin are given every half hour for a maximum of 18 drops.

Forty-seven cases treated by this procedure were analyzed. In 87 per cent the therapy was successful. The fetal death rate was 6 per cent, but only one of three fetal deaths can be attributed to the induction of labor. There were no maternal deaths, and the morbidity rate was 10 per cent.

J. P. GREENHILL.

Colmeiro-Laforet, C.: The Diagnosis of Rupture of the Amniotic Sac, *Rev. espan de obst. y ginec.* 2: 99, 1945.

In reporting 450 tests of the acidity of the vaginal fluid by means of indicator paper, the author found that 95 per cent were in the normal range of acidity. Marked deviations from the normal range were found in cases of premature rupture of the amniotic sac.

J. P. GREENHILL.

## Newborn

Vahlquist, Bo: Serum Iron and Serum Bilirubin in Congenital Anemia of the Newborn and Icterus Gravis Neonatorum, *Upsala Läkareförenings Förhandlingar Ny Följd. Femtionde Bandet* 183, 1945.

The author gives a brief but clear résumé of the importance of the Rh factor determination, and also stresses the fact that the Rh mechanism does not cover all cases of congenital anemia of the newborn and icterus gravis neonatorum.

His present study is based on four patients with congenital anemia of the newborn and five patients with icterus gravis neonatorum. The serum iron and serum bilirubin content are noted in each case using the Jendrassik-Cleghorn method. He discussed the value and limitations of the Van den Bergh test, and has drawn a conclusion that in the newborn the Van den Bergh test is of no assistance in differentiating between hepatogenic and hemolytic jaundice. His results are discussed in this most informative article.

JAMES P. MARR.

Wilmer, Harry A.: Two Cases of Periarthritis Nodosa Occurring in the First Month of Life, *Bull. Johns Hopkins Hosp.* 77: 275, 1945.

The author summarizes the article as follows:

Two cases of periarthritis nodosa, one dying at ten days of life and the other at thirty-seven days, are reported as the youngest cases in the literature. In one case there was an umbilical infection; in the other there was a large inflammatory-necrotic mass involving the right adrenal containing large numbers of unidentified cocci.

rhago often require blood transfusion, there is evidently danger of incompatible transfusion, except in institutions where Rh tests are made on all expectant mothers, or where there is a blood bank of only Rh-negative blood.

HARVEY B. MATTHEWS.

Davis, L. J., and Forbes, William: *Thiouracil in Pregnancy—Effect on Fetal Thyroid*, *Lancet* 11: 740, 1945.

The authors report the case of a 21-year-old woman who had had one previous normal pregnancy, following which she developed evidence of thyrotoxicosis. She was started upon treatment with thiouracil, 600 mg. being given daily. Following successful therapy the dosage was reduced to two hundred milligrams daily and continued at this dosage level of five and one-half months, at which time she became pregnant. The dosage was further reduced to two hundred milligrams on alternate days. During the sixth month of pregnancy she complained of a severe headache which persisted for two days, and at which time she suddenly became cyanosed, collapsed, and died.

Examination of the thyroid gland of the fetus revealed it to be enlarged and hyperplastic as compared with a presumably normal gland from a premature infant, and it showed histologic evidence of considerable functional activity. It resembled the gland of an adult receiving too much thiouracil.

The authors concluded that administration of thiouracil to pregnant women, and probably to nursing mothers, demands caution.

CARL P. HIRSH.

Lagererantz, Carl: *Electrophoretic Analysis of Serum in Pregnancy and in Pregnancy Toxemia*, *Uppsala Lakareforenings Forhandlingar* 117, 1945.

Electrophoretic analysis of serum from nonpregnant, normal pregnant, and pregnant women with toxemic symptoms have been performed. The analysis showed

1. The x- and B-globulins increase both relatively and absolutely during normal pregnancy.
2. The albumin and total protein decreases during normal pregnancy.
3. Women with toxemia have both a relatively and absolutely larger x-globulin than normal patients.
4. There is no significant difference in the electrophoretic patterns of umbilical cord serum after a normal pregnancy and after a toxemic one. Umbilical cord serum shows small x- and B-globulins.

An account of earlier work on x- and B-globulins is given, and the probable nature of the raised x- and B- globulins during pregnancy and in cases of toxemia is discussed.

JAMES P. MARR.

Gosende, J. C., and Sandiano, R. O.: *Chorea and Pregnancy*, *Bol. Soc. de obst. y ginec. de Buenos Aires* 23: 798, 1944.

The authors report a case which they consider to be true chorea of pregnancy. The disease appeared between the seventh and eighth months of pregnancy in an 18-year-old primipara. A detailed study of the heredity, family, and individual history revealed no record of predisposing causes. The authors maintain that true chorea of pregnancy may occur when the toxins of pregnancy affect a susceptible patient.

J. P. GREENHILL.

Monckeberg, C.: *Hypertension in Pregnancy*, *Rev. méd. de Chile* 73: 193, 1945.

The author finds that, while in normal pregnancy arterial pressure is normal, a slight increase during the latter part of the period is also normal, and during labor increased blood pressure due to effort is to be expected. Otherwise all cases of hypertension during pregnancy must be considered pathologic, either a chronic state temporarily aggravated, or an acute state produced by the pregnancy and by the complex glandular disturbances not yet well understood.

J. P. GREENHILL.

Vinson, Porter P.: *Cardiospasm in the Newborn*, J. Pediat. 27: 565, 1945.

The author defines cardiospasm as persistent dysphagia, with x-ray evidence of obstruction to food at the cardiac end of the esophagus without organic stenosis. He reports such a case, and stresses the value of concentrated food orally and adequate amount of fluid subcutaneously as the treatment of choice.

JAMES P. MARR.

De La Villa, L., and Nieto, J.: *Study of the Deviations From the Normal Weight-Curve of the Newly Born and an Investigation of Their Causes*, Rev. espan. de obst. y ginec. 2: 11, 1945.

The authors observed 1,500 newborn living children for at least ten days after birth and found 204, or 13.9 per cent, with deviations from the normal weight curve. The deviations were classified in seven distinct curve types. The curve of greatest frequency, 26 per cent of the total deviations, represented a prolonged initial decline of weight, and a slow recovery. The most marked curve of deviation which showed no recovery of weight included 8.8 per cent of the total deviations, and included the three patients which did not survive. The illnesses of the mother which were correlated most closely with these deviations were infections and heart disease; other pathologic factors were premature labor, congenital weakness, syphilis, intracranial hemorrhage, and jaundice. It was not possible to establish any correlation between these deviations and the type of nourishment of mother or child.

J. P. GREENHILL.

### Pregnancy, Complications

Burch, A. E.: *The Association of Erythroblastosis Foetalis and Accidental Antepartum Hemorrhage*, J. Obst. & Gynaec. Brit. Emp. 52: 463, 1945.

All cases of antepartum hemorrhage occurring at St. Alfege's Hospital between February and June, 1945, were studied for Rh factor. In six cases of placenta previa, the Rh reports are available for only five, and in all these the patient was Rh-positive. In five cases of accidental antepartum hemorrhage, the mother was Rh-negative and the father Rh-positive; in one other case of accidental antepartum hemorrhage, the mother was Rh-positive, and in another both mother and father were Rh-negative. In one case of antepartum hemorrhage, placental insertion not determined, the mother was Rh-positive. Thus five out of ten of the mothers who had accidental antepartum hemorrhage were Rh-negative with Rh-positive husbands; and in three of these women anti-Rh agglutinins were demonstrated in the blood. In the three cases in which the patient was delivered soon after the occurrence of the hemorrhage, there was one child with jaundice who recovered without transfusion, one with gross hydrops, and one stillbirth, possibly as a result of the course of labor. In the two cases in which the patient was delivered some weeks after the occurrence of the hemorrhage, the fetus in each case was stillborn, macerated, and of a size indicating death at the time of the onset of bleeding. In two of the cases with Rh-positive mothers, the Rh genotypes were determined; the mothers were found to be Rh<sub>2</sub> rh and Rh<sub>1</sub> rh, and the children Rh<sub>1</sub> Rh<sub>2</sub> in each case so that it is possible that less common antibodies were present in the mothers, but this was not demonstrated. It is also noted that two of the three cases of erythroblastosis foetalis occurring in six months at Queen Charlotte's Hospital, there was premature separation of the placenta with antepartum hemorrhage.

While this series of cases is small, the findings suggest that women in whom isoimmunization can occur are abnormally prone to accidental antepartum hemorrhage, and that the resulting damage to the placenta may be a factor in the transmission of antigen and antibody. In some cases there seems to be an association between the time between bleeding and delivery and the severity of the erythroblastosis and the titer of the agglutinins. The risk to the baby from erythroblastosis in such cases may be greater than the risk from prematurity, so that induction of labor rather than expectant treatment may be indicated, but whether this is the case is as yet impossible to say. Since women with antepartum hemor-



## Correspondence

### Early Diagnosis of Anencephaly

*To the Editor:*

In the April, 1946, issue of the *Journal* there appeared an article on page 571 by Dr. Catherine W. Blumberg and Dr. George Tepliek entitled "Early Clinical and Roentgenologic Diagnosis of Anencephaly." I believe that it is worthy of comment.

The opening sentence reads, "The importance of early diagnosis of fetal monstrosities cannot be too greatly stressed, as it precludes the possibility of unwittingly allowing the patient thus burdened to progress to term." Why? If their management of the case is what they advocate, I should think it would be worth reconsidering. Labor was induced at six months with rupture of the membranes. This was followed by infection of the amniotic sac necessitating the use of penicillin. Then, to add injury to the insult, the cervix was manually dilated from 1 to 2 cm. to 3 to 4 cm. Finally, "after dilatation" (full?), "the macerated anencephalic fetus was extracted with some difficulty."

I cannot see why the life and health of the mother should have been jeopardized for the sake of the premature delivery of a dead baby. Why not let Nature take its own course—and in a much safer manner? I may be wrong, but I think the above treatment was an exceedingly hazardous way of handling a minor obstetric difficulty.

GEORGE SPECK, M.D.

2806 SOUTH RANDOLPH STREET  
ARLINGTON, VA.  
MAY 13, 1946

### Reply by Dr. Blumberg

*To the Editor:*

Dr. Speck's chief criticism appears to be the management of the case we reported. Apparently it was not noted that, following diagnosis, the patient was referred for further care, since the U. S. Public Health Service Dispensary does not have facilities for prenatal care or delivery. We do not wish to enter upon controversial discussion of obstetric management, but, in defense of the obstetrician who handled this case following our diagnosis, we wish to state that his willingness to submit a summary of the progress and management in order that we might make a complete case report for publication was greatly appreciated and indicates to us that he did not feel a need for justifying his procedure.

A policy to "let Nature take its course" is contrary to the basic need for specialized obstetric training to care for those cases in which Nature's course is abnormal. By letting natural forces dictate management a "minor obstetric difficulty" may become a major one. Two of the patients cited in our report carried their pregnancy three or four weeks beyond term, and one of them was finally delivered by cesarean section.

Applying the principles of good medical practice, we reaffirm that early diagnosis of abnormal conditions, and the prevention of greater complications should be our goal. Opinion may differ as to the advisability of terminating a pregnancy where the fetus is dead, and possibly abnormal, but the final opinion can be rendered in any specific case only by the doctor in attendance.

CATHERINE W. BLUMBERG, M.D.

WASHINGTON, D. C.  
AUG. 7, 1946.

### Pregnancy, Physiology

Koloszynski, F. W.: A Short Study of Histaminase Activity During Pregnancy, J. Obst. & Gynaec. Brit. Emp. 52: 426, 1945.

A method for the quantitative estimation of serum histaminase was worked out from the Kapeller-Adler test based on a qualitative method in which  $H_2O_2$  produced by the action of histaminase on histamine decolorizes the dye indigo-disulphonate. Three modifications of the Kapeller-Adler method were employed: air was used instead of oxygen; the time of incubation was 72 hours; the degree of decolorization was measured by an Evelyn photoelectric colorimeter and expressed in mg. of dye per 1 ml. of serum. It was found that two important factors influenced the decolorization of the dye in this test: (1) nonspecific activity associated with incubation; (2) specific histaminase activity associated with incubation and the presence of histamine in the serum-dye mixture. The test was employed on the sera of 12 nonpregnant women, 40 pregnant women, and nine with pre-eclampsia. The nonspecific activity was the same in all three groups. No evidence of specific histaminase activity was found in the sera of the nonpregnant women. There was definite evidence of histaminase activity in the sera of pregnant women; this activity was low in the first 100 days of pregnancy and high after that time. The sera of patients with pre-eclampsia also showed histaminase activity: no evidence of the inhibition of either nonspecific activity or histaminase activity was found in these cases. Further investigations are needed to determine the function of histaminase in pregnancy; the author suggests that this enzyme may be an important link in the metabolism of histidine during pregnancy.

HARVEY B. MATTHEWS.

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### Necrology

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THOMAS WATTS EDEN, M.D., F.R.C.P., F.R.C.O.G., of London, eminent Obstetrician, gynecologist, teacher, editor, and author, Honorary Fellow of the American Gynecological Society, died Sept. 22, 1946, at the age of 83 years. Well known as editor of the *Journal of Obstetrics and Gynaecology of the British Empire*, prominently identified with the development of the Chelsea Hospital for Women to an outstanding institution, playing a great part in placing abdominopelvic surgery on a firm foundation, a major in the R.A.M.C. in the first World War, chairman of the committee which developed the scheme for a national midwifery service, and author with Lockyer of a widely used textbook, he was widely recognized as an outstanding member of his specialist group. Upon delivering an address before the American Gynecological Society at its annual meeting in 1920, he was made an honorary member of this body.

## Items

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### Third American Congress on Obstetrics and Gynecology

St. Louis has been chosen as the meeting place of the Third Annual Congress on Obstetrics and Gynecology, to be held September 8 to 12, 1947. Further particulars will be announced in later issues.

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### American Board of Obstetrics and Gynecology, Inc.

#### Examinations

The next written examination (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 7, 1947, at 2:00 P.M. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held in Pittsburgh, Pa., June 1 to 7, 1947. All applications must be in the office of the Secretary by Nov. 1, 1946. All candidates, especially those in military service, are requested to keep the Secretary's Office closely informed of changes in address.

Several changes in Board regulations and requirements were put into effect at the last annual meeting of the Board held in Chicago, Illinois, from May 5 to May 11, 1946. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. Candidates are again notified that they must expect to be examined in both branches of the specialty of obstetrics-gynecology. The Board considers that at least fundamental training and knowledge of both branches of this united specialty are essential, regardless of the fact that a candidate may in his practice major in one or the other branch. At this meeting the Board also ruled that it will not accept the nine months' residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration, April 1, 1946.

Applications for the 1947 examinations cannot be accepted after Nov. 1, 1946. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

PAUL TITUS, M.D.

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The following diplomates have been certified and are added to the previously published list: Dr. David A. Conners, 131-07 86 Road, Richman Hill 18, N. Y.; Dr. Joseph Deutsch, 55 E. Washington St., Chicago 2, Ill.; Dr. Robert Wade King, Permanente Foundation Hospital, 280 MacArthur Blvd., Oakland 11, Calif.; Dr. Edwin Vance Lawry, 300 Homer Ave., Palo Alto, Calif.; Dr. Sim Bedford Lovelady, Mayo Clinic, Rochester, Minn.; Dr. William Harvey Mease, 813 Fayette Title & Trust Bldg., Uniontown, Pa.; Dr. Samuel A. Manalan, Morrison Field, West Palm Beach, Fla.; Dr. Edison Lloyd Russell Schram, 870 Wellington St., London, Ontario, Canada; Dr. David Jennings Werner, 4810 N. Newhall Street, Milwaukee, Wis.; Dr. Emanuele Momigliano, 2357 W. Madison Street, Chicago, Ill.

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#### Erratum

In the September issue of the JOURNAL on page 528, under Items, the address of Dr. Herbert Malone Black was stated in error. The correct address is 1401 Taylor Street, Columbia, S. C.

## Lactobacillus Therapy in Vaginitis Due to Trichomonas

To the Editor:

Everyone who has studied the biology of the vagina knows of the symbiosis between the normal and pathologic flora of microbism there; the relationship between the normal vaginal bacillus and the lactobacillus; and the dependence of these bacilli from glycogen contents of the vaginal epithelium.

Last year, L. Brady and R. D. Reid described in the JOURNAL\* a new therapy with lactobacilli in cases of vaginitis due to trichomonas. In so doing they completely overlooked that the same therapy was detected and described about twenty-five years ago and published in the *Zentralblatt für Gynäkologie*, 1920 (Gynaecological University Clinic, Charité, Berlin). What is still more interesting, they used nearly the same methods as the author did long ago: They cultivated the lactobacilli in practically the same way, they gave the same food to these bacilli in order to survive in the vagina the attacks of the pathogenic microbes, they put about one million of these lactobacilli in one tablet—as did the author twenty-five years ago, and they had the same good results in about 70 cases, whereas the author published his results in 250 cases twenty-five years ago.

At that time the living lactobacilli compressed into a tablet of milk sugar were already on the market, called "Bacillosan," and other articles on the same subject were published in medical journals.

As I was very much interested to see my old ideas revived absolutely in the same way with such a striking resemblance in detail—identical twins cannot resemble each other more—I can assure Brady and Reid they will have the same excellent results as I had so long ago.

There is one snag only in this therapy. After years and years the lactobacilli no longer grow in the same strength on the culture medium, and they very often lose the power to grow in a hostile alkaline vaginal medium and to overwhelm the antagonistic trichomonas. They can no longer produce the normal vaginal pH., so that the good results of the beginning become weaker.

Should Brady and Reid repeat the experience in years to come, they will certainly bear in mind the publications of other authors.

ALFRED A. LOESER, M.D.

2 DEVONSHIRE PLACE, LONDON, ENGLAND.

SEPTEMBER 25, 1946.

## Reply by Drs. Brady and Reid

To the Editor:

When we first conceived the idea of using lactobacillus therapy in the treatment of vaginitis due to *Trichomonas vaginalis*, we surveyed the literature for previous publications on the subject. Unfortunately, we overlooked the paper published by Dr. Loeser in the *Zentralblatt für Gynäkologie*, 1920, but are glad to have this belated opportunity to call attention to Dr. Loeser's work.

We believe that the measures we are taking will prevent the changes in our cultures that Dr. Loeser refers to in his letter. In the laboratory, we are selecting for the lactobacillus tablets only those strains of lactobacillus which produce consistently large amounts of acid and which are unusually resistant to storage. As a matter of fact, our records in the laboratory clearly show that not only have the number of organisms in the tablets been markedly increased, but also the viability of the organisms has been prolonged during our five years' study of this problem.

LEO BRADY, M.D.

ROGER D. REID, M.D.

BALTIMORE, MD.

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\*Lactobacillus Therapy in Vaginitis Due to Trichomonas, AM. J. OBST. & GYNEC. 50: 509, 1945.

Long ago, wise men divided the faculty of medicine into three somewhat vague but major components, priestcraft, art, and science, and it is the varying ratio of these three factors in the teaching and understanding of medicine which has produced the type of doctor and of practice during the ages.

With the emergence of man from the Cro Magnon phase, the healing art was controlled by the priests and medicine men almost entirely, and divine aid was the only medication to which they had recourse. Incidentally, should one doubt the efficacy of treatment by suggestion and by the intervention of supernatural factors, one need only to observe the effects a Navahoe "sing."

However, even during this era, an attempt at art appeared because the Shamans and the priests sought to reinforce their appeals to godly therapeutics by prescribing the most nauseous and repellant mixtures to be ingested by their patients while the elaborate ceremonies of the ritual appeal to the gods were going on.

There remain many vestiges of these priestly times in the medicine of today. In many schools, the Hippocratic oath is still solemnly read to a partially awed but mostly cynically amused graduating class. Generally the reader rather diffidently interrupts himself to explain that all of the statements of prechristian credo are not to be understood literally, but that idealistically and historically the oath is of some vague but unquestioned merit.

Then, too, there may be noted the remnants of a sort of phallic worship of the uterus in the veneration of this viscus still entertained by some of our modern gynecologists. To ablate this sacred organ except upon the most drastic indication is to sacrifice it and to commit some sort of offense, though against whom or what does not seem to be disclosed. One may note that other organs of the female cosmos are not at all revered, and the thyroid and gall bladder are eradicated with no compunction whatever. Only the uterus, "the birth mother," is surrounded by these ancient taboos.

The tenacity with which theistic dogmas persist in medical thought is revealed by the insistence of certain sects that the spiritual welfare of their communicants outweighs all bodily disabilities. The refusal to permit the termination of pregnancy, even though the mother is in imminent peril of her life should gestation continue, and the general acquiescence of the profession in this dictum in deference to the will of the spiritual advisor rather than the obvious and real need of the patient is still all too common. Slowly, however, all of these atavisms are fading in the light of reason and scientific thought.

The transition of medicine from the primitive state to its comparatively rapid development as a realistic art coincides with the emergence of the Greeks and the Hellenic mind. These people pursued the study of medicine objectively from the practical side and paid scant attention to philosophical speculation. As Riesman well says that little can be added to the picture of disease left us by the Hippocratic school—their power of description kept pace with their power of observation. This objectivity is pre-eminently a Greek quality and, in addition, they had a generally sane attitude toward Nature; their master minds taught medicine, not magic.

With the conquests of Rome, medicine and, indeed, all things concerning pure art or scientific reasoning suffered a great decadence, and had it not been

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### PRESIDENTIAL ADDRESS\*

#### The Ways of Doctors and the Practice of Physic

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IN THIS year of grace, one planning to compose an essay finds at his disposal a vast wealth of subjects of transeendent importance, all stemming from possibly the most stupendous exhibition of man's usual unfortunate activities since our first forefathers descended from their arboreal perches. The war in general, postwar America, Europe, Asia, the atomic problem, and, should he desire to be local in his effort, the growing economic strife, socialized medicine, the future trend of education; these and countless other topics offer themselves to his pen. In deference to the intellectual stature of this Society and the dignity of his office, your speaker has surveyed these various themes, seeking for that one which would contribute to the annals of the Society a most noble and everlasting epic. But, as subject after subject was considered, scrutinized, and pondered, it soon became evident that beyond an introductory paragraph or two, nothing further seemed to happen. He possessed just too little accurate knowledge, and pride prevented your essayist from wishing to emulate the Judge in Wolfville Days of whom the old cattleman said, "The colonel is just an ordinary liar and you can listen to him. But the Judge, he is something beyond Nature, for whenever he opens his mouth there is a diminution in the sum total of human knowledge."

So we descend from the clouds, sadly abjure the opportunity to "elegantly enstate our erudition" and present a homely little dissertation upon the ways of doctors, and the practice of physic.

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NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

in health and disease, suddenly there appear on the bookshelves and in the medical journals portentous essays upon what is euphonistically entitled psychosomatic medicine, and lo! the wheel has turned full circle and we are back at the beginnings with suggestion and ritual again the dominant forces, and with our ancient priestcraft reappearing in a leading role. With a difference, however, it must be confessed.

During the several ages when medicine was first one thing and then another, the relationship of the doctor to the public and the esteem and respect in which the physician was held fluctuated almost in direct ratio with the realism and search for truth or the mumbo jumbo with which doctors ornamented their profession. Thus, among the Greeks and the Egyptians, the medical man was respected as a scholar and a little feared as possessing perhaps a too intimate acquaintance with the force of black magic.

Later, in the decline of Rome, the physician had sunk to a deplorably low estate, and was in part a sort of servant, in part a healer. From early times, and often during the Middle Ages, medical attendants frequently suffered physical punishment and even death if they failed to cure their patient. It is told that Astragosilde, Queen of France, on her deathbed, begged her husband, Gontrano, to throw her doctor out of the window immediately after her death, which was done with the greatest punctuality (Reisman).

As of this time, conditions among medical men are not quite so perilous, we being merely mulcted of our savings by malpractice suits rather than suffering floggings, flayings alive, or other cheerful diversions of an earlier and more artless epoch. More lately, the doctor has regained his high estate, and is in general regarded as an important and authoritative member of the community.

If one reflects upon the uneven progress of medicine down the years, one is arrested by the manner in which the profession has been engaged continuously and conscientiously in an untiring effort to encompass its own destruction.

That the effort has failed, at least in considerable measure, is due not to any lack of zeal on our part, but to the stubborn refusal of Nature to reveal certain secrets concerning the mechanism of disease and to the inability of fallible human intellects to penetrate the recesses of biology deeply enough to obtain this knowledge.

It would seem no great exaggeration to say that if every research problem now in progress in every laboratory in the world were to be solved suddenly and correctly, that medicine, as we know it, would cease to exist, at least for practical purposes.

When the cause of a disease is understood, prophylaxis against its development becomes automatic, so that it is fair to assume that once complete knowledge is attained the function of the practitioner of medicine will be reduced to the supervision of births, the management of lesions due to trauma, and the amelioration of the distresses attending senescence and decay. To this one might add, and a gleam of hope is offered by the suggestion, that there would remain so many persons either too stupid or too indolent to avail themselves of prophylaxis; this group being of such large proportion (at least in a world where the present system of private medicine prevails) that a considerable

for the Arabian School which maintained high standards, the profession might well have been completely degenerated into mere charlatanry. However, even with the curious exorcism of astrology which came to medieval Europe chiefly through the Arabians and the Arabists, it was this group which preserved many of the Greek texts and to whom modern medicine owes so much.

Slowly and painfully (to patient as well as to the toiling student) the art of medicine began to develop in a rational fashion. Indeed, this epoch coincides rather closely with the general rise of rationalism in Europe. The obstetric forceps began to supplant the ingeniously devised syringes for the baptism of the unborn child, the ligature replaced the hot pitch application to control hemorrhage, and the rudiments of pharmacology began to appear. Before too long the art and craftsmanship of the physician had reached a high level, and naturally there arose acrimonious controversies as to the superiority of one method of procedure over another. Some of these disputes gave rise to the most eloquent and satisfying polemics, indeed, many of them would do credit to any ultramodern professional disagreement. Next came the period of instruments of precision, the discovery of bacteria as factors in disease and the development of organic chemistry. These first steps toward the making of medicine an exact science, more or less, have been followed by ever-lengthening strides until one might almost conjecture that, by study with precision methods alone, absolute diagnosis might be attained without the doctor ever having seen the patient, but having simply digested the findings of various investigations.

This scientific age brought with it that curious period of therapeutic nihilism during which the great exponents of medicine expressed no interest whatsoever in the amelioration of the sick persons suffering, sharply decried the administration of drugs to relieve mere symptoms, and insisted upon a complete and perfect diagnosis to be confirmed, if the patient was so obliging, by the results of autopsy.

It was in this period of development that the absurd reverence for the history of the case, the anamnesis, arose. Years ago some snuffy, dry-as-dust German professor enunciated the doctrine that the history of the case was the very keystone of diagnosis, and that this document increased in value in direct ratio to its verbosity. This dictum was eagerly absorbed by the native and foreign students of the period and was soon brought to America where, with our passion for mass production, case histories soon became veritable encyclopedias of misstatement.

The almost sacred process of so-called complete history taking was so impressed upon the student and intern that hospital records especially, in the more highly organized institutions, are often volumes of confused and largely imaginary accounts of the past ills and the genetic misfortunes of over-articulate and under-intelligent persons.

Indeed, even an accurate and correct anamnesis is of very minor importance in the diagnosis and management of disease, but in many schools this whole subject is surrounded by an aroma of sanctity, almost ritual.

While precision methods are steadily being expanded and more and more exact mathematical formulas begin to be employed in evaluating body function



These unaccountable lags in observation are mentioned, not in a disparaging sense, but merely to emphasize the remarkable development of medicine as a whole. The advances in our knowledge of biology in its broadest sense are awe-inspiring, and in no other field of human endeavor have investigation, experiment, and logical thinking eventuated in such a vast array of known and proved facts.

Consider now the graduate in medicine as he firmly clutches his diploma, that magic scroll before which the doors of practice open wide, and prepares to return to the renter thereof his hired cap and gown. His mind is an intellectual miscellany of the assorted facts and theories with which it has been crammed for four long years, and he is greatly occupied as to his accumulated knowledge in reducing chaos to mere disorder.

He has been taught a bit of priestcraft, more of the art of medicine, and a vast deal of abstract science, a reasonable amount of which is not at all true. How is it possible, one asks oneself, that a man so prepared can face the grim task of healing the sick which lies before him?

The answer is very simple. The ills to which the flesh is heir cannot be sorted out and catalogued as to which require the purely academic biological approach, which demand art, and which priestcraft; but most diseases are in themselves, a melange of mechanical failures, to be managed by art, errors in metabolism, or body chemistry which fall into the domain of pure science and a vast inchoate mass of psychic maladjustments and mental aberrations which are only amenable to priestcraft in its highest sense.

So that our doctor, himself a compound of these three great facilities, is excellently well equipped to deal with the manifold problems of human illness far better than he could possibly be were the groping ideas of our Aesculapian forefathers to be discarded in medical teaching and replaced by pure experimentally proved facts.

There remains the question as to how well this diverse teaching has been carried out, how well the student has been prepared to absorb the information he receives, as well as how he stands in regard to general culture including familiarity with the humanities without which his horizon is and must inevitably remain, narrow and merely technical.

It is an ill thing to analyze one's fellow craftsmen critically, and surely not a safe or wise method of acquiring merit, yet what has to be said, must be said.

Doctors, as a professional unit, are definitely lacking in general culture. Of course, countless individual physicians have attained pre-eminence in the liberal arts and have made distinct contributions in all of the ramifications of cultural endeavor. However, this is not true of the profession in the mass.

Should a bassoon player in the orchestra unfortunately rupture a blood vessel in the course of his Aolian exertions, it would generally be quite difficult to requisition a physician from the audience to administer first aid, but should the conductor of the symphony engage in fisticuffs with his "concert meister," the stage would instantly be crowded with a whole posse of lawyers eager and prepared to manage the necessary legal procedures. The same con-

army of doctors would be necessary to minister to their ills. This universal willingness to sacrifice its own rewards and emoluments in the interests of the general health is one of the noble attributes of our profession in which the humblest student may well take pride.

Despite the thousands of keen eyes, sharp ears, and alert minds that have been employed in attending the sick, it is amazing how so many seemingly obvious facts not only of pathology, but of anatomy and physiology, too, managed to escape attention for so long.

In some instances this lag is wholly inexplicable, in some it is due to the authoritative opinion of certain distinguished physicians who have daunted discoveries by devastating discussion, and sometimes by lazy and indifferent observation by those who, like Mark Twain's description of Fenimore Cooper, "deal freely in important omissions."

Among the inexplicable delays is the matter of the fetal heart sounds. The heaving, distended abdomen of the gravid woman has ever been a source of unending interest and speculation to those with whom she is in intimate contact. Husbands, friends and neighbors, midwives, doctors, all love to observe and comment upon this phenomenon, and yet it was not until 1828 that Mayer of Geneva was able to announce the fact that the fetal heart tones not only could be heard through the maternal abdominal wall, but the heart rate might actually be counted.

Assuming that the first pregnant woman became an object of family concern some 50,000 years ago, this item of gestational physiology seems to have been overlooked overlong.

To find a truth and have it repudiated and neglected by the leaders of the profession is one of the bitter things for the discoverer, and often an incalculable calamity for the world. In 1827, Melier, a young intern in a Paris hospital, expressed the belief that inflammation in the right iliac fossa depended upon disease of the vermiform appendix. He reported undoubted cases of appendicitis confirmed by autopsy. He described gangrene, perforation, concretions, and peritonitis. He sought to make it possible to diagnose inflammation of the appendix, and believed that if the diagnosis could be made, operation was demanded.

The great Dupuytren arose in discussion and destroyed that young surgeon.

For over half a century the profession followed Dupuytren, who was wrong and rejected Melier, who was right; and scores of thousands died who might have been saved.

The man who had the truth was no more heard of in surgery. His further life history is unknown, and he disappeared into oblivion.

How all too common are such ill-considered acts by men who have attained great eminence but who possess in high degree the ability to draw mathematically precise lines between unwarranted assumptions and foregone conclusions.

The great controversy regarding the infectious nature of puerperal fever belongs in the same category, although here there is also much slovenly thinking; but whether or not the work of Sister Margaret Kenny in the management of poliomyelitis is another example of the same sort, deponent saith not.

Then there are the four-year premedical courses, especially designed for those proposing to enter the field of medicine. These are as varied as the minds of the faculty groups who arrange them and, while in one college the emphasis is placed upon biology and allied matters, in another it may be organic chemistry, while some occupy the semester hours with anatomy, bacteriology and so on, all of which are repeated immediately the student begins his actual medical course.

This type of preliminary work simply accentuates the vocational training, later to be so greatly amplified in the school of medicine.

Insufficient, true formative education, together with the quite casual manner with which the student considers his intellectual obligations to himself, would seem to offer a fair explanation of our low cultural standards.

Happily, the correction of this somewhat depressing state of affairs offers but little difficulty, although perhaps a strong conviction on the part of the writer of the ease of bringing about the desired change, may have oversimplified it in his mind.

Either the University of Montpellier in about 1350, or that of Cologne a little later, set forth the conditions under which a degree of bachelor of arts might be conferred. A term of four years, each of two semesters, was the minimum requirement, and ever since this time, colleges and universities have continued the practice under identical conditions.

However, with the passage of the years, and especially since the "educational revolution in America" of the late eighties, and since the wide application of the elective system in our colleges, the amount of work required to obtain the various academic degrees has been steadily reduced, although the time elapsed remains constant.

In effect, then, rather than that the student be fully occupied to attain his education in four years, he is much concerned with social and athletic activities in order to fill his days.

The result is a very superficial structure of mental development, with a deterioration of the ability to concentrate and acquire the mental discipline so absolutely requisite for successful training in a profession.

These leisurely and so often unfruitful years are followed by the crowded curriculum of the medical school in which there is scarcely ever time for even a brief survey of correlated topics, not definitely related to medicine itself.

It is proposed that an entirely different educational program in colleges be inaugurated for such students as propose to pursue a professional career—be this medicine, law, engineering, or whatever.

There could be established a two-year course in cultural education, the work to be entirely completed within this time and the student graduated, with perhaps some academic recognition in the form of a new degree.

The subjects taught would include history, philosophy, the classics, languages, especially English, mathematics, and literature, with possibly a secondary group, as logic.

There would be no attempt to deal with either abstract or applied science unless one regards mathematics as a science rather than a philosophy. The roster would require many more hours in the classroom than at present, possibly

dition prevails in most cultural fields, and it is rare that one is beguiled by informed and interesting conversation when in the company of a group of doctors.

How uncommon it is to find members of our profession devoting themselves to great national and world problems (other than those concerned with health) when it would seem that their intimate and personal contacts with so many persons must give them a deep insight into the aspirations and needs of people as a whole.

When a doctor utters such libelous attacks upon his own colleagues he lays himself open to Sidney Smith's description of the bishop. Smith said he could never reconcile himself to a belief in the Apostolic Succession until he met the bishop of Bath and Wells, and found in that individual physical and spiritual attributes so absolutely identical with those possessed by Judas Iscariot that he could no longer doubt the truth of the direct descent, one from the other.

It becomes imperative that one making such sweeping statements as the foregoing should be able to justify, or at least to offer some reasonable and applicable explanation.

To say that a lack of general culture among doctors is due to their inferior intellectual stature is manifestly absurd, since no man not far above the average in mental ability could hope to survive the rigors of a medical education, and one need only point to the power of inductive reasoning which characterize scientific research and the solution of the confusing and intricate problems which fall to the doctor to prove conclusively that the physician's mind is in general far above the average.

It has been suggested that the exigencies and fatigues attendant upon the practice of medicine leave no time for cultural activities, but this does not seem to hold true, because taken by and large, doctors do have leisure, at least for golf and bridge. There must, then, exist some other reason, and this would seem to lie in certain deficiencies in the education of the physician, deficiencies which are true in all countries but which are especially notable in America.

Mindful of this condition, medical educators have sought to correct it by demanding a certain amount of liberal arts study as a prerequisite to entrance into the medical school.

Most of our universities now require two years of college work, while some insist upon the possession of the degree of B.A. or B.S. Though the theory is excellent, in practice the present plan leaves very much to be desired. The freshman and sophomore years in most of our colleges are mainly occupied in stimulating the indolence acquired by the student during his senior year in high school, while the so popular elective system enables him to choose those courses which are best suited to leaving his mind at absolute rest.

Intellectual curiosity is not often awakened and, where only the first two years of college are required, the men have generally only partially completed any comprehensive courses they may have undertaken, and have not acquired much facility for scrutiny and analysis of their subject matter.

## HYDRAMNIOS\*

### The Joseph Brettauer Memorial Lecture

LOUIS CARNAC RIVETT, M.D., LONDON, ENGLAND

FIRST of all, I want to tell you how much I appreciate the very great honor you have conferred on British gynecology and on me personally by inviting me to come to this great country to deliver the Joseph Brettauer address. I feel the honor is even greater by the fact that it has been made a second time, the first time being somewhat unpropitious for travel, at any rate for those of us who were then on the other side of the Atlantic Ocean.

I have chosen as my subject for this address, "Hydramnios." Pundits tell me the word is really "hydramnion," but I am going to persist in using the more common, although possibly inaccurate word, "hydramnios."

In 1933, at the Congress of Gynecologists and Obstetricians of the British Empire, held at Birmingham, I read a short paper describing a few cases and advocating the general adoption of the treatment that I had found successful. Although many obstetricians seem to have heard of this treatment, I find exceedingly few ever use it, and I am hoping, as a result of this paper, to spread the gospel somewhat.

Hydramnios is vaguely defined as being a great excess of liquor amnii. Most authorities say that the normal amount of liquor amnii is about 1 to 2 pints (600 to 1,200 c.c.), but it has never been definitely laid down exactly how much must be present before the transition from excessive liquor to hydramnios takes place. From a practical point of view, the exact amount is not important, as the condition of hydramnios is usually such an enormous excess that there is no doubt at all. I think no one will quibble if I define it as when the amount of liquor exceeds 5 pints (3,000 c.c.).

Many suggestions have been put forward as to the cause of this great excess of liquor. In roughly 50 per cent of cases we find gross fetal maldevelopment, anencephaly, spina bifida, stenosis of the esophagus, hydrocephaly and twins, this last one being common and usually associated with two normally developed babies. We are still left with about 50 per cent of cases in which we can find no cause whatsoever. In one well-known manual of obstetrics, edited by Eardley Holland,<sup>1</sup> it is stated that when hydramnios occurs in a sac of one of twins, there is no doubt that the source of the excessive liquor is fetal urine,<sup>1</sup> but no evidence whatsoever is produced of the grounds on which this very unlikely opinion is founded.

I have tried injecting indigo, carmine, and insulin into the amniotic sac and looking for evidence that either was absorbed by the mother, and failed to find any.<sup>2</sup> DeLee<sup>3</sup> administered methylene blue to the mother and found it appeared in the fetal urine, but not in the liquor amnii.

\*Presented at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

thirty-six or even forty hours weekly, this to be determined by trained educators. Since the medical student habitually spends considerably more time than this in his daily work, the intensity of such a course would develop in the student the ability to study and the so necessary mental discipline referred to before.

Our absurdly long vacations could well be shortened, the months of July and August being generally the only period when the heat of summer makes mental or physical concentration difficult in America.

One can visualize the graduate of such a course of study as a man who has been given an insight into the thoughts and practice of foregoing generations and who has learned the proper method of study and who happily has had the golden gates of the world's literature opened to him. Now, stimulated and eager, our student enters medical school, not for four years, but for six, the total period of university life thus remaining unchanged.

The first two years of the medical course would be in effect a transition between the cultural studies which have preceded it and the definitive medical work to follow. Psychology, sociology, genetics and the laws of heredity, general biology with comparative anatomy and physiology, and many other subjects germane to medicine and of inestimable value to the doctor would be taught by highly qualified scientists.

The beginnings of the basic sciences would be incorporated in this first two years, after which the usual medical curriculum would follow for the remaining four years.

By such a plan, many of the present gaps in the mental equipment might well be eliminated and the resulting product, it is hoped, would be a physician of far wider horizons, capable of acute cultural analysis such as now belongs only to the few.

This whole matter of medical pedagogy is so fascinating that it is difficult to close its discussion.

The prevalent view, for example, is that if a man of outstanding investigative ability be secured to head a department, the institution obtaining his services is fortunate. Sometimes this is true, but more often such a man surrounds himself with like-minded persons, and while the research work proceeds apace with admirable results, the pedestrian, dull teaching of undergraduate students the facts of medicine, is often neglected to an unbelievable degree.

Despite any opinion to the contrary very, very much of medical knowledge consists of apparently unrelated facts which, to be known, must be studied and memorized, and in which no amount of inductive reasoning is of any avail whatsoever.

The necessity of training teachers of medicine to teach is very real—and is far too casually considered not only in America, but in Europe as well.

The suggestions here made may be the idle dream of an old fellow whose teaching days have long gone by but, if there has been expressed but the tiny germ of an idea which may stimulate wiser heads to give it some thought and perhaps to amplify it to a usable plan, he will remain well content.

In most cases the excess of liquor will reaccumulate in three or four weeks, and the whole procedure can be repeated again and again. Some cases do not produce further hydramnios and I do not know why. I saw one patient about thirty weeks pregnant, and withdraw nine pints of liquid. Nine weeks later she had a normal spontaneous delivery of a normal live baby. I saw another case in 1942, a primigravida 25 years of age, whose last menstrual period had been twenty-one weeks previously. She complained that during the past two weeks her abdomen had increased enormously in size, and she was in great discomfort. On palpation, the uterus reached to the ensiform cartilage, and the abdomen measured 36 inches in circumference at the level of the umbilicus. An x-ray disclosed twins but, as this early stage of pregnancy, it was not possible to determine whether or not fetal abnormality was present. Seven pints of liquor were withdrawn. Three weeks later she was again in great discomfort, and I withdrew 9 pints. Four weeks later I withdrew 11 pints, and six weeks later again 11 pints; a total of 38 pints (23 liters). Ten days later she went into spontaneous labor, thirty-six weeks after her last period, and had a normal labor; the first twin weighed 2 lb., 7 oz. (1,170 Gm.), and was stillborn, having obviously died during labor, as evidenced by early maceration; the second twin weighed 3 lb., 9 oz. (1,710 Gm.), cried spontaneously, and did well. Twenty-eight days later the baby was discharged, weighing over 5 lb. (2,400 Gm.).

*Dangers and Difficulties.*—I have been told that this method is very dangerous. There is a risk of carrying virulent infection into the uterine cavity. There is a risk that the trocar and cannula may perforate the mother's intestine and set up fatal peritonitis. There is a risk that the large blood vessel in the uterine wall may be perforated and cause hemorrhage. There is a risk that the trocar and cannula may seriously injure the fetus (perforate an eye for instance). There is a risk that the placental attachment may be separated with serious bleeding. Not one of these things has occurred. It is far easier to surgically sterilize the skin of the abdominal wall than it is to sterilize the vaginal vault and cervix. It is unknown to find intestine in front of a uterus of this size unless it is tethered there by adhesions from a previous operation, and anyway it is easy to detect it if it is there by simple palpation and percussion. I have pricked blood vessels on several occasions, the only trouble I have found is when I withdraw blood-stained liquor or even blood, which tends to clot in the needle. There have been no ill-effects that could be shown due to this accident at all. Palpation and selecting an area where fetal parts are not immediately under the uterine wall remove any chance of injuring the fetus. Separation of the placenta has probably occurred in one or two cases as a stillborn baby is eventually born and the placenta is found to be extensively fibrosed—so in my experience these theoretical dangers do not actually ever occur.

### Results

After eliminating cases in which the first aspiration was performed later than thirty-five weeks' gestation, I find that live babies resulted in over 25 per cent of cases which required some treatment before viability of the fetus. In all

*Incidence.*—Hydramnios occurs about once in two hundred pregnancies. It has been estimated as occurring in anything ranging from one in one hundred to one in three hundred, but usually the estimates are made on a comparatively small series when a variation of one or two may make a very great difference to the answer. It appears most commonly to be found between the twentieth and twenty-eighth week of gestation, but in some cases the great excess does not cause maternal distress until the last four or five weeks. When the amount of liquor exceeds 5 pints (3,000 c.c.), it is likely to cause marked maternal distress, not only physical discomfort, but cardiac and respiratory embarrassment and edema and, rarely, albuminuria, and it is usually obvious that something must be done. I find the usual treatment everywhere is to puncture the membrane through the cervical canal, either by direct puncture or by high puncture with a metal catheter. This method is not always successful as, when hydramnios affects one of twins, it is always the sac which is lying in the upper part of the uterus that becomes distended, and puncture of the membrane of the nonhydramniotic sac does not give immediate relief, but only produces the second effect of interference via the cervix, namely, the onset of labor. As the majority of cases occur before viability of the fetus, this method of treatment inevitably kills the baby or babies.

In 1912, Wormser<sup>4</sup> in Germany described that he had punctured an amniotic sac via the abdomen—not in a case of hydramnios. In 1933, I published a paper<sup>2</sup> in which I described a method of treating hydramnios by puncturing the amniotic sac and withdrawing the excessive liquor. The method is as follows: about one hour before the procedure,  $\frac{1}{8}$  grain of omnopon and  $\frac{1}{150}$  grain of scopolamine are administered and the patient kept quietly in bed. A spinal trocar and cannula is prepared (I use this instrument as I find its length, 3 inches, is about right, and it has a fairly large bore). A collecting bottle, lengths of rubber tube, and a suction pump are also required. With the patient lying on her back the abdomen is palpated and an area chosen, usually above the umbilicus, where there is marked fluctuation and where fetal parts cannot be palpated. The skin is prepared over this area by painting with iodine. A skin puncture is made with a small tenotomy knife and the cannula inserted through the abdominal wall, through the uterus, and into the amniotic sac. On withdrawing the trocar it can be observed that the liquor is very rarely under pressure, it usually drips out quite slowly, so the cannula is attached to the suction pump via the collecting bottle and as much liquor as possible is withdrawn.

The most I have withdrawn at one operation was twelve and one-half pints—over a gallon and one-half, or seven and one-half liters. The patient was much more comfortable after it and did not go into labor, and later had a normal live baby. When no more liquor can be withdrawn, the abdomen is palpated to ascertain whether or not there is still an excessive amount and, if so, the trocar and cannula are inserted in a different place and more withdrawn. When no more can be withdrawn, a dressing is applied and the patient is returned to her room; one-fourth of a grain of morphia is administered and repeated that evening and again the following morning, to discourage uterine contractions. A certain number of cases do go into labor: a certain number do not.



## CORPUS CARCINOMA

### A Study of Three Hundred Twenty-Two Cases\*

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*(From the Department of Obstetrics and Gynecology, University of Michigan)*

PHYSICIANS charged with the responsibility of treating carcinoma patients in large numbers are constantly seeking to improve existing therapeutic methods with the hope of prolonging the survival period. For nearly half a century hysterectomy has been accepted as the preferred treatment for corpus carcinoma. The results from operation alone were generally viewed with optimism, the impression being—and it was only an impression—that hysterectomy offered an extremely favorable prognosis. With the advent of follow-up studies this optimism gradually dwindled. Incomplete hysterectomy was proved unsatisfactory and total hysterectomy is now recognized as no cure-all in these cases. About 1925 radium was replacing radical hysterectomy as the preferred method of treatment for cervix cancer. Because of its successful use in this connection, it was also tried in corpus carcinoma. But, since its use was largely confined to advanced cases, it is not surprising that the results were equivocal. While irradiation did not cure many advanced cancers of the uterine body, the fact that it prolonged life and cured some was important. That corpus carcinoma could be seriously damaged and occasionally destroyed by the use of radium, x-ray, or both, had now been demonstrated. From these early experiences came the seeds from which grew the methods of combined therapy in use today. Since this early trial period many excellent contributions on the subject have appeared in the literature, and we regret that lack of space and time does not permit their well-deserved recapitulation in this report. Because early experience foreshadowed definite benefits from irradiation in the management of corpus carcinoma, this whole problem was carefully considered by us in 1931 at the time our Gynecology Tumor Conference was first organized. As a result of our deliberations, a preferred program of treatment was outlined. The plan was based on the following assumptions.

1. Elimination of the primary neoplasm could probably best be achieved through complete surgical extirpation of the entire uterus, tubes, and ovaries.

2. Theoretically, supplemental irradiation therapy should be most beneficial when given prior to operation. By so doing we hoped to: (a) cause widespread damage to cancer cells; (b) minimize manipulative spread at the time of operation; (c) obliterate lymphatics (something which now, fifteen years later, we know is only partially accomplished).

3. Since we were not depending upon irradiation for destruction of the primary lesion, and since a damaging effect on outlying cancer cells was our aim in using preoperative irradiation, it was agreed that deep x-ray therapy followed

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these cases, relieving the tension by puncture of the membrane via the cervix would inevitably have brought on labor with death of the fetus.

In conclusion, there is obviously much room for research into the cause or causes of hydramnios.

In the few cases in which I have had an Rh negative factor, it seems to have no bearing at all.

In view of the fact that at any rate a certain number of babies' lives can be saved, I do ask you all to give this method of treatment a fair trial. My series is only about 50 cases. That is really too small for a final pronouncement, and in this country it should not take long to get sufficient numbers to prove its value or otherwise.

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The radium factors were:

Brass tandem applicator of either two or three chambers depending on the length of the uterine canal. Total filtration was equivalent to 0.5 mm. of platinum. Each chamber might contain from 30 to 50 mg. of radium. The radium dose per chamber varied from 1,500 to 2,400 mg. hr., the lower part of this range was employed when a two-chambered tandem was used, and the higher part with a three-chambered tandem. Occasionally, vaginal applicators placed in the lateral fornices were also used.

Many things influence the results of treatment and all deserve mention. In this connection it was of interest to learn whether, as a result of cancer education, patients were consulting physicians earlier than formerly. As shown in Table II, our study revealed no recent improvement in this respect.

TABLE II. TIME WASTE FROM ONSET OF FIRST SYMPTOM TO BEGINNING OF TREATMENT

REPORTED BY	YEAR	TIME WASTE
Miller <sup>1</sup>	1929	24.0 months
Collins <sup>2</sup>	1934	11.1 months
Miller <sup>3</sup>	1940	12.7 months
Miller and Henderson (this report)	1946	12.5 months

The average time lapse from the onset of symptoms to the beginning of treatment is significant. Corpus carcinoma occurs most frequently in women past the menopause, the average age in our series being 54 years. Consequently, the appearance of spotting or abnormal discharge at the average age of 54 years should be sufficiently unusual to cause concern. Apparently there still is great need for cancer education among women of this age group. This time waste factor, though significant, does not always indicate the extent of the lesion.

While clinical grouping of these cases is not very satisfactory, helpful information may be gained by determining uterine size, a tangible factor which serves as the criterion for most clinical classifications of corpus carcinoma. The clinical grouping of 301 patients in our series is shown in Table III.

TABLE III. CLINICAL GROUPING OF 301 CORPUS CARCINOMA CASES

TREATMENT	GROUP I		GROUP II		GROUP III		UNKNOWN	
	NUM-BER	PER CENT	NUM-BER	PER CENT	NUM-BER	PER CENT	NUM-BER	PER CENT
Radium	6	16.2	24	64.8	7	18.9	0	0
X-ray	5	15.6	11	34.2	6	18.7	10	31.2
Radium and x-ray	25	28.0	45	50.5	15	16.8	4	4.4
Surgery	2	10.0	10	50.0	8	40.0	0	0
Radium and surgery	5	31.2	8	50.0	3	28.8	0	0
X-ray and surgery	40	41.6	50	52.0	6	6.1	0	0
Radium, x-ray and surgery	3	27.2	5	45.6	3	27.2	0	0
Total	86		153		48		14	

Our clinical classification was based on the following:

Group I.—No palpable enlargement of uterus.

Group II.—Moderate enlargement of the uterus up to the size of a two-and-one-half-month pregnancy.

Group III.—A large uterus—the size of a three-month pregnancy or greater.

later by adequate surgery should be our planned treatment of choice. The decision to use preoperative deep x-ray therapy in preference to radium was based on its known effectiveness in cervix neoplasia and its helpfulness in prolonging life in some ovarian carcinomas. Furthermore, we believed that the broader fields affected by the use of irradiation might also damage neoplastic cell masses sometimes found in the tubes and ovaries of corpus carcinoma patients (seven times in our operated cases).

During the fourteen and one-half years since the inception of this program of treatment in 1931, we have had under our care 322 patients with corpus carcinoma. All these individuals have been carefully studied, and data concerning their treatment and progress recorded on punch cards suitable for statistical evaluation in International Business Machines. All patients have been traced, there are no untraced cases.

Since the University of Michigan Hospital is a State-owned institution primarily for the care of indigent patients from outlying districts, it is obvious that many of our corpus cases were advanced and beyond surgical help when admitted. These advanced patients, and others considered excessively poor operative risks, were treated entirely by irradiation usually a combination of x-ray and radium.

TABLE I. METHODS OF TREATMENT USED IN THE CARE OF 322 PATIENTS WITH CORPUS CARCINOMA

TREATMENT	A		B					
	NUM- BER	PER CENT OF TOTAL	SURVIVAL RATES IN PER CENT OF THOSE ELIGIBLE					
			3 YEAR		5 YEAR		10 YEAR	
			NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT
None	21	6.5						
Radium	37	11.4	34	44.1	29	41.3	10	30.0
X-ray	32	9.8	30	23.3	22	27.2	6	16.6
X-ray and radium	89	27.4	65	33.3	50	28.0	26	23.0
Surgery	20	6.2	18	66.6	15	53.3	8	50.8
Radium and sur- gery	16	4.9	14	87.5	13	86.6	9	81.8
X-ray and surgery	96	29.5	79	84.7	61	77.0	23	65.0
X-ray, radium and surgery	11	3.6	7	70.0	4	66.6	3	60.0

Ninety-six, or 29.5 per cent, were treated according to plan; namely, preoperative deep x-ray therapy followed in six weeks by adequate surgery. This represents the largest treatment group in this series.

The type and the number of patients in each category are shown in Table I.

The factors generally used in the x-ray treatment were as follows:

Two hundred kilovolt peak radiation filtered by 0.5 mm. copper and 1.0 mm. aluminum, half value layer (h.v.l.) 0.9 mm. copper, distance, 50 cm. minute output about 50 roentgens as measured in air. Two anterior and two posterior pelvic fields 12 by 15 cm. to 15 by 15 cm. in size. The beam was directed at an angle through each field so as to cross-fire the uterine corpus. Two hundred roentgens as measured in air were given to each of two fields daily to a total dose of 2,000 to 2,200 roentgens per field.

TABLE V. CARCINOMA OF THE CORPUS UTERI\*  
INTRAUTERINE RADIUM

REPORT BY	NUMBER TREATED	PER CENT FIVE-YEAR SURVIVALS
Heyman	186	35.5
Fricke and Bowing	16	50.0
Fricke and Heilman	76	52.6
Healy and Brown	64	58.0
Hurdon	40	62.0
Corscaden	27	48.0
Total	409	

46.4

\*Modified from J. A. Corscaden, J.A.M.A., Dec., 1944.

TABLE VI. CARCINOMA OF THE CORPUS UTERI\*  
HYSTERECTOMY

REPORT BY	NUMBER TREATED	PER CENT FIVE-YEAR SURVIVALS
Pleiderer	153	51.5
Von Mikulicz and Volbracht	133	54.1
Norris and Dunne	115	47.8
Masson	306	66.6
Total	707	

57.8

\*Modified from J. A. Corscaden, J.A.M.A., Dec., 1944.

TABLE VII. CARCINOMA OF THE CORPUS UTERI  
RADIUM FOLLOWED BY HYSTERECTOMY

REPORT BY	NUMBER TREATED	PER CENT FIVE-YEAR SURVIVALS
Healy and Brown	93	55.0
Heyman	65	78.0
Ward and Sackett	21	57.1
Newell and Crossen	19	63.2
Morton	18	61.1
Arneson	10	90.0
Corscaden	25	72.0
Total	251	

65.3

\*Modified from J. A. Corscaden, J.A.M.A., Dec., 1944.

sure—the prospects appear very promising. In 1936 Arneson<sup>7</sup> reported a 90 per cent five-year survival rate for corpus carcinoma following the use of intracavitary radium and surgery. Scheffey, Thudium, Farell, and Hahn,<sup>8</sup> also report a 90 per cent five-year survival rate following the use of radium and surgery.

These are truly amazing figures, especially since death from natural causes in women of average corpus carcinoma age might well be enough materially to influence survival rate during a five-year period: Were it not that both reports are based on a small number of cases, it would appear that we need search no further for an entirely satisfactory treatment. When, however, collected results obtained from the preoperative use of radium followed by surgery are reviewed, the picture is not nearly so striking (Table VIII).

While our own experience with the use of preoperative radium in corpus cases has likewise been good, the number of cases so treated is again too small to permit conclusions. In sixteen patients so treated, there were 86.6 per cent five-year survivors. (See Table I.B.)

TABLE IV. HISTOLOGIC GRADE—301 CASES CORPUS CARCINOMA

TREATMENT	GRADE I		GRADE II		GRADE III		GRADE IV		NOT GRADED	
	NUM-BER	PER CENT	NUM-BER	PER CENT	NUM-BER	PER CENT	NUM-BER	PER CENT	NUM-BER	PER CENT
Radium	1	2.7	19	51.3	14	37.9	1	2.7	2	5.4
X-ray	0	0	9	28.1	16	50.0	2	6.2	5	15.6
Radium and x-ray	2	2.2	51	57.3	25	28.0	6	6.6	5	5.5
Surgery	2	10.0	14	70.0	4	20.0	0	0	0	0
Radium and surgery	2	12.5	9	56.2	3	18.7	1	6.2	1	6.2
X-ray and surgery	2	2.0	58	60.4	32	32.2	2	2.0	2	2.0
Radium, x-ray and surgery	1	9.2	5	45.4	5	45.4	0	0	0	0

The histologic grade is shown in Table IV.

While histologic grading of endometrial carcinoma does not necessarily indicate prognosis, experience has shown that there is some difference in the rate of growth, invasiveness, and spread between the less-differentiated and the highly-differentiated carcinomas. Histologic grade, therefore, is a factor in determining survival rate.

In evaluating results of treatment, it should be noted that our survival rates are uncorrected. In studies involving older patients such as this, correction for noncarcinoma deaths will some day be desirable. This is not yet done customarily, and was not done in this report.

There appears to be little reason for more than passing consideration of our cases treated by irradiation alone. In the groups so treated were the advanced cases, the extremely obese patients, and, of course, the very poor surgical risks. The fact that in these groups treated by means of irradiation it was possible to attain approximately a 20 per cent ten-year salvage rate is significant and reason for recognizing in irradiation therapy, be it intraeavitary radium or x-irradiation, a potent and valuable adjuvant to surgery in the management of corpus carcinoma. This fact was clearly shown in a compilation of results by several workers reported by Corseaden<sup>4</sup> in 1944. Tables V, VI, and VII are modified from Corseaden's report, and deal with operable cases. They indicate what may be expected by the various therapeutic methods or combinations thereof.

While there appears to be no objection to the combined preoperative use of both x-ray and radium, in the past most studies have dealt with only a single form of preoperative irradiation. Perhaps this is fortunate, since it permits better evaluation of their respective merits when used in this connection. That both forms of irradiation can be extremely helpful in the control of corpus carcinoma has been frequently demonstrated.

In 1941 Wintz<sup>5</sup> reported a five-year survival rate of 69.1 per cent in 127 operable cases treated by x-ray alone. In the same year Hurdon<sup>6</sup> announced a 62.0 per cent five-year salvage rate in 40 patients treated with radium alone. While these are selected figures and probably represent the most optimistic results obtained from the use of these therapeutic weapons, the literature abundantly attests the effectiveness of irradiation in the control of corpus carcinoma. Used alone, neither radium nor x-ray appears to equal the results obtained by surgery, but when combined with surgery—especially as a preoperative mea-

6. The use of very high voltage x-ray as a preoperative measure in corpus carcinoma appears promising and should be explored further.

7. Radium, likewise, gives good results, but, on the basis of available data, we do not believe the relative merits of preoperative x-ray versus radium can be accurately stated.

8. We hold no special brief for any form of therapy. Our interest in and work with deep x-ray as a preoperative measure in corpus carcinoma was entirely with the hope of increasing our survival rate.

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### Discussion

DR. J. MASON HUNDLEY, JR., Baltimore, Md.—This discussion is based upon a study of 93 patients at Johns Hopkins Hospital with adenocarcinoma of the corpus uteri. We have divided these patients into two groups, namely, those that are poor and those that are good surgical risks. The reason for this is quite obvious, for the debilitated, elderly patient is treated with irradiation alone while those in the good risk group receive a course of intracavitary radiation which is followed by a panhysterectomy and a bilateral salpingo-oophorectomy.

The plan of procedure in the poor risk group is as follows: Diagnosis is determined by careful curettage of the body so as not to disseminate infection which is frequently associated with the malignancy. The size of the uterus is then determined, for the enlarged uterus as a rule bespeaks advanced disease with myometrial involvement. Several sacs of radium, each containing 25  $\mu$ g., are then introduced into the uterus until the cavity is filled; four to five sacs may thus be used. These sacs are removed in an order in reverse to their introduction, for otherwise a so-called "log jam" may occur and thus render their removal difficult. This difficulty occurred in one patient necessitating the removal of the radium under pentothal anesthesia. These debilitated poor risk patients receive, as a rule, 4,000 to 4,500 mg. hr. of radium. Following this the patient is given a cycle of deep x-ray therapy through four portals to the amount of 8,000 roentgens. We have reviewed 46 patients that were so treated, and find that the salvage rate at the end of four years and seven months is 28.3 per cent.

The method of therapy and results of patients in the good risk group which number 47 is as follows: the preliminary phases of therapy, i.e., dilatation and curettage, pathologic diagnosis, and intracavitary radiation are the same as in the poor risk patient, the dosage of radium applied in multiple sacs being 4,000 to 4,500 mg. hr. Approximately four to five weeks later a panhysterectomy and bilateral salpingectomy are done. An important and well-recognized preliminary step is clamping the isthmus portion of the Fallopian tubes so as to prevent expulsion of malignant cells into the peritoneal cavity. After intracavitary radiation, how soon should the panhysterectomy be performed? This is a moot point. We feel that lines of cleavage are dissipated and the tissues become more fibrous and less workable if we delay longer than four to six weeks. It would seem that intracavitary radiation does increase somewhat the operative difficulty but, in spite of this, we have had no operative accidents, i.e., bladder or ureteral fistulas, nor have we had an operative death. In this good risk group we have reviewed 47 patients treated by this combination method of therapy and

TABLE VIII. COMPOSITE TABLE SHOWING SURVIVAL RATES FOLLOWING DIFFERENT FORMS OF TREATMENT FOR CORPUS CARCINOMA\*

TREATMENT	NO. OF CASES	SURVIVAL RATE IN PER CENT	
		5 YEAR	10 YEAR
Surgery	707	57.8	
Radium	409	46.4	
Radium and surgery	251	65.3	
X-ray and surgery	96	77.0	65.0

\*Compiled from Corscaden's report and our own data.

For reasons already stated, our treatment of choice during the past fourteen and one-half years has been deep x-ray therapy followed by surgery six weeks after completion of the x-irradiation. Results achieved by this combination based on 96 cases are shown in Table I-B, and for convenience are repeated here, thus:

84.7 per cent three-year survivors.  
 77.0 per cent five-year survivors.  
 65.0 per cent ten-year survivors.

Table VIII represents an attempt to compare results by the several methods of treatment now in common usage. Obviously, the inequality in the number of cases in the various groups lays this comparison open to criticism.

There was one postoperative death among our 96 patients treated by preoperative x-ray and surgery. This occurred on the tenth day and was due to pulmonary embolism.

The uterus, tubes, and ovaries of these 96 patients were abundantly blocked for study purposes. Fifteen, or 15.6 per cent, revealed no carcinoma. This is less than has been reported following the use of intracavitary radium (24 per cent to 75 per cent), but it should be recalled that we did not depend upon irradiation for destruction of the primary lesion.

The effectiveness of intracavitary radium is variable and inconsistent. Gray, Friedman, and Randall<sup>9</sup> have shown that the carcinoma may persist even after very heavy treatment with radium.

While the significant factual data of our study have been stated, there remain the impressions—thoughts which bud during every study only to disappear or else grow into something more than an impression—the fruits of experience.

To list them is to risk being dogmatic. Even so, this is the way things appear to us:

1. Preoperative x-ray has proved to be a valuable adjuvant to total hysterectomy and bilateral salpingo-oophorectomy in the treatment of corpus carcinoma.

2. Its use clears up uterine infection, reduces uterine size, and decreases pelvic hyperemia, thereby facilitating operation.

3. Preoperative x-ray has not in any discernible way interfered with wound healing.

4. The three weeks required for its administration is a drawback, but by no means a serious one, since for most patients this is an outpatient procedure.

5. The results obtained from preoperative x-ray warrant its continued use, at least until some other combination or new form of therapy is proved more satisfactory.



spread sepsis. One of these patients died from such infection after the application of radium. One died from a lung abscess three and a half months after operation. Therefore, x-ray alone is preferable under such conditions as a preoperative treatment. But our feeling at the present time is that preoperative radiation is most important, and that radium should be given as well as x-ray in most cases.

DR. L. C. SCHEFFEY, Philadelphia, Pa.—Since the work of our clinic at Jefferson was presented before the Obstetrical Society of Philadelphia this spring and the paper published in the JOURNAL (52: 529, 1946), I shall refer only briefly to our experience at this time, quoting from several of our tables.

*Table I* refers to the patients seen, treated, and followed up, showing that 104 are eligible for five-year statistics.

*Table II* refers to the results obtained with a planned technique of preliminary intra-uterine radium followed by total hysterectomy and bilateral salpingo-oophorectomy, eight to twelve weeks later. We do not feel that the preoperative radium destroys the malignancy locally; in fact, over 50 per cent of the removed uteri show residual carcinoma. We are convinced, however, that the lesion is devitalized as shown on the photomicrographic slides; that this lessens the chance of cancer-cell distribution at the time of operation, and that vaginal vault recurrence is less likely, for we have seen none to date. Neither has there been any primary mortality in the series.

Whether preliminary radium is preferable to preliminary x-ray is debatable. We would not hesitate to use x-ray postoperatively if there is evidence of extension from the uterus at the time of operation. In this series, no x-ray was used either preoperatively or postoperatively. There will be certain cases, of course, in which the size of the uterus and the contour of the endometrial cavity, particularly where concomitant myomas are present, that preclude the application of intrauterine radium units. In such instances we have proceeded immediately with total hysterectomy and adnexal removal, either with a frozen section report of the curettage, or merely with a suspicion of fundal carcinoma being associated with the uterine myomas.

*Table III* shows the comparative results obtained with (1) surgery alone (adequate and inadequate); (2) irradiation alone (radium and/or x-ray); (3) an unplanned technique (surgery, adequate or inadequate, combined with radium and/or x-ray in varied sequence); (4) the planned technique (as shown in *Table II*). The superiority of the latter, at least in our hands, seems striking.

The survival figure after irradiation corresponds fairly closely with the figures showing the percentage of previously irradiated uteri with residual carcinoma. This offers some consolation to ourselves and to the patient in those instances where irradiation has to be relied upon, because subsequent operation is contraindicated for well-known reasons. In other words, irradiation alone seems to offer a 40 to 50 per cent chance of five-year survival when surgery is impossible or inadvisable.

The notation regarding primary mortality needs some explanation. There were two deaths in 87 patients in whom surgery played a part in treatment, either alone or in conjunction with irradiation; in 8 of these patients it was not possible to remove the uterus at operation. Of the remaining 79 patients, the uterus was removed, but five of the 79 patients had received either primary or subsequent treatment elsewhere, leaving 74 patients who were treated solely at Jefferson. This accounts for the slight variation in the mortality percentage which is based solely on the same two deaths among the entire group of 87 patients not receiving the planned technique of treatment displayed in *Table II*, and shown for comparison in *Table III* with no primary mortality.

DR. GEORGE GRAY WARD, New York, N. Y.—Since 1919, we have had under our direction at the Woman's Hospital 243 cases of carcinoma of the corpus uteri.

We believe surgery is the most important factor in the treatment of this disease. Irradiation is a valuable adjunct. Preoperative irradiation is the most desirable technique. The question as to whether it is better to use irradiation in the form of radium or deep x-ray is open to discussion.

we find that at the end of four years and seven months we have a survival rate of 76.7 per cent. This figure vividly demonstrates the advantages of intracavitary radiation plus pan-hysterectomy over irradiation therapy alone.

All of the 93 patients reviewed had a microscopic grading and we found that the majority fell in the grades II and III and, as expected, the more anaplastic the growth, the more quickly it disappeared.

A recent report by Stowe (*AM. J. OBST. & GYNEC.* 51: 57, 1946) on residual growth in the uterine musculature following adequate intracavitary radiation is most illuminating. He reported 53 patients with corpus carcinoma who had been treated by the above-mentioned combination method of therapy, and found that 50.9 showed residual carcinoma in the myometrium. He was of the opinion that operative removal of the organ was of vital importance.

At present we are restudying the radiated uteri, and the examination of multiple sections may confirm Stowe's report.

We prefer intracavitary radiation, for we feel that the radium applicator can be directly applied to the lesion. However, the results presented by Dr. Miller show that equally good results may be obtained with the use of deep x-ray therapy.

DR. FRANK A. PEMBERTON, Boston, Mass.—Up to 1936 we treated 294 of a total of 307 cases of carcinoma of the endometrium at the Free Hospital for Women. Varying sequences of x-ray, radium, and operation, as well as operation alone, were used. There are not enough cases in each group to make useful comparisons, but the total results are shown in the tables below:

Total	307	Five-year salvage	55.7 per cent
Treated	294	Five-year salvage	58.1 per cent
Total eligible		Ten-year salvage	43.5 per cent
Treated eligible		Ten-year salvage	45.4 per cent

From 1936 to 1941, 108 cases were treated with the following results:

X-ray and radium	No. 27	Five-year salvage	12 (45 per cent)
Hysterectomy, radium, and x-ray	No. 66	Five-year salvage	43 (66 per cent)
Hysterectomy	No. 15	Five-year salvage	9 (60 per cent)
Total	No. 108	Five-year salvage	64 (59 per cent)

In the first series there was a five-year salvage of 58.1 per cent, and ten-year salvage of those eligible of 45.4 per cent. The five-year salvage in the second series is about the same. The figure of 45 per cent for the cases treated by radiation alone is rather high, but is due to there being several early cases in these patients who are poor risks. We operate on every case where it is possible.

Twenty-eight of these 66 patients had hysterectomy first, then radium in the vagina, and x-ray externally; intrauterine radium followed by operation and x-ray in 23; and intrauterine radium followed by operation in fifteen. Bilateral salpingo-oophorectomy was always combined with the complete hysterectomy. There were 15 cases in which hysterectomy alone was done, with a 60 per cent five-year survival.

Now it seems reasonable that if these 66 cases and those treated by operation alone had all received radiation before operation, the results would have been better.

Since Healy's report in 1939 of a 79 per cent five-year salvage in 28 cases so treated, and Miller's report in 1940 of his success with preoperative x-ray, we have used preoperative radiation more extensively, and our impression is that the results are more favorable.

We feel that intrauterine radium as well as x-ray should be preferable to x-ray alone, because there is bound to be some squeezing of the uterus during operation, even though it is held by clamps down the broad ligaments and never with a double hook or uterine clamp on the fundus. The cells are devitalized if enough radium is given. They get from 3,000 to 5,000 roentgens of x-ray. The intrauterine radium should devitalize the cells of the local growth, and there should be less chance of spreading them during the manipulations.

An objection to the use of intracavitary radium is that if the tumor is infected or there is enough stenosis of the cervix to have caused pyometra, the application may stir up and

## CLINICAL AND PATHOLOGIC ASPECTS OF PRIMARY SARCOMA OF THE UTERINE TUBE\*

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THAT primary sarcoma of the uterine tube is an unusually rare lesion is borne out by the fact that thus far only 21 cases have been specifically mentioned in the literature throughout a period of sixty years. Little detailed information exists in gynecologic texts. Furthermore, it is an unusual coincidence that Senger reported the first case in 1886, in the same year that Orthmann called attention to the first authenticated primary carcinoma of the tube. Since then, approximately 578 tubal carcinomas have been reported, a ratio to tubal sarcoma of about 25 to 1. Secondary sarcoma of the tube is even less frequently mentioned.

My interest (L. C. S.), and that of our former resident, Dr. Warren R. Lang, in this uncommon condition, was initiated by personal experience with such a patient, who was first seen by Dr. Fred B. Nugent. The case history is presented herewith.

### Case Report

C. K., aged 70 years, para i, gravida i, was admitted to the private gynecologic service of the senior author at Jefferson Medical College Hospital on March 6, 1944. She complained of low pelvic pain and sensitivity, with intermittent vaginal discharge, sometimes bloody. The family history was essentially negative. Appendicectomy with drainage had been performed in 1932. Apart from "heart trouble," noted several years prior to admission, there were no acute or serious illnesses in the past.

The menopause occurred in 1929 at the age of 55 years. A sudden hemorrhage, rather profuse, occurred in May, 1943. The patient consulted Dr. Fred B. Nugent of Reading, Pa., and he performed diagnostic curettage at the Reading Hospital in June, 1943, and an intrauterine application of 1,200 mg. hr. of radium was administered. Dr. E. D. Funk, Director of Laboratories, reported the scrapings as follows: "The endometrium is atrophic and consists of a fibrous connective-tissue stroma with a paucity of straight nonsecretory glands. There is no evidence of malignancy. Microscopic diagnosis, atrophic endometrium."

The patient reacted well to this treatment, but continued to have an intermittent bloody vaginal discharge. She also complained of a "bloated feeling" in the abdomen, and had difficulty with urination. External irradiation, or further radium therapy to control the persistent but slight bleeding, was suggested as a therapeutic measure several months later, but discouraged by Dr. G. W. Chamberlain, Roentgenologist at the Reading Hospital, who favored surgical treatment, rather than further irradiation.

\*Read at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

Microscopic examination of the growth is essential for an accurate diagnosis, and a suction biopsy or a diagnostic curettage is necessary to procure the tissue. Suction biopsy may fail to reveal a small area of carcinoma in the cornua or in an irregular cavity. A proper curettage is less likely to give a negative finding. I prefer to do a curettage, and at the same time take advantage of the opportunity to introduce radium to render the tumor cells inactive as soon as possible. Should a six-hour report be negative, the radium may be removed at once, otherwise, 2,400 to 3,600 mg. hr. are given. A complete hysterectomy and salpingophorectomy follows in from two to four weeks, after which a series of deep x-rays is given by the Coutard technique, which takes from twenty-five to thirty days.

It seems to me that there is less delay by using a radium application first, except in cases where the disease has extended beyond the uterus and an hysterectomy is not feasible.

In 1942, I gave a report of our five-year survivals in 142 cases of corpus carcinoma. The absolute survival rate was 44.4 per cent. Since then we have had a five-year follow-up of 38 cases. Of these, 21 are alive and well, and there were 17 deaths, or an absolute survival rate of 55.2 per cent. In the 17 deaths, eight were considered favorable for irradiation and hysterectomy. Nine were in advanced stages of the disease with metastases and unsuitable for operation, from senility, diabetes, or cardiovascular disease, etc. Of the eight favorable cases, two lived five years, but died of cancer.

In the advanced cases, one died of coronary thrombosis two months after radiation and one died of acute appendicitis.

The proportion of advanced cases seen in a series influences the absolute survival rate. Each patient with carcinoma of the corpus uteri must be individualized and treated according to the conditions present to obtain the best results.

DR. GEORGE KAMPERMAN, Detroit, Mich.—I would like to discuss a limited series of cases. Within the last month I saw in my office patients treated for carcinoma of the uterine fundus during 1938. All were of the number one clinical group with the uterus about normal in size. We do not obtain a microscopic grading from our pathologist because he does not believe the grading is accurate. We do believe the clinical grading judged by the clinical extent of the disease is most important, and at least equally important to the microscopic grading. When we speak of wanting to get our patients early, I believe we really refer to the clinical grading.

Of the eight patients personally operated upon and managed during 1938, seven are alive and well without symptoms or signs of recurrence. One patient developed ascites and other evidence of recurrence and died within one year of operation and treatment. We believe that those who do die from recurrence of the carcinoma are likely to die early, and, if they survive a few years without recurrence, the prognosis immediately is good.

Our method of treatment at Harper Hospital is this: We like to employ preoperative radiation with both radium and x-ray. In each case we individualize and consult our radiotherapist. The intrauterine dosage of radium is never less than 3,600 milligram hours. A very fleshy patient may be given a larger dose of radium, since we do not feel so confident about the efficacy of x-ray in a fleshy patient. The x-ray radiation is administered by a supervoltage machine, 600,000 voltage constant. The deep x-ray therapy is given over a period of four or five days, and not over a period of three weeks as used by Dr. Miller. We are cognizant of the criticism of large radiation doses in some clinics. We are not, however, afraid to use large dosage and believe the nature of the disease justifies heroic measures. After hysterectomy, which is performed about eight weeks after the preliminary radiation, a second course of deep x-ray therapy is given.

adnexal enlargement was firmly attached to the posterior layer of the broad ligament and to the infundibulopelvic ligament. There was no gross evidence of peritoneal implants of any sort, and no regional nodal enlargements could be palpated; neither did the liver feel abnormal. The appendix had been removed previously, and postoperative adhesions in this area, as previously noted, were not disturbing.

An operative diagnosis of subacute pelvic inflammatory disease with left pyosalpinx, resultant from previous irradiation therapy with radium, was recorded. No thought of malignancy was entertained. Complete hysterectomy with bilateral salpingo-oophorectomy (Richardson technique) was carried out uneventfully. Eight Gm. of sulfanilamide were placed in the cul-de-sac, and the abdomen closed in routine fashion. No drainage was employed.

Postoperative convalescence was satisfying and uneventful. There was little morbidity, the patient was allowed out of bed within two weeks, and she was discharged from the hospital on March 31, 1944.

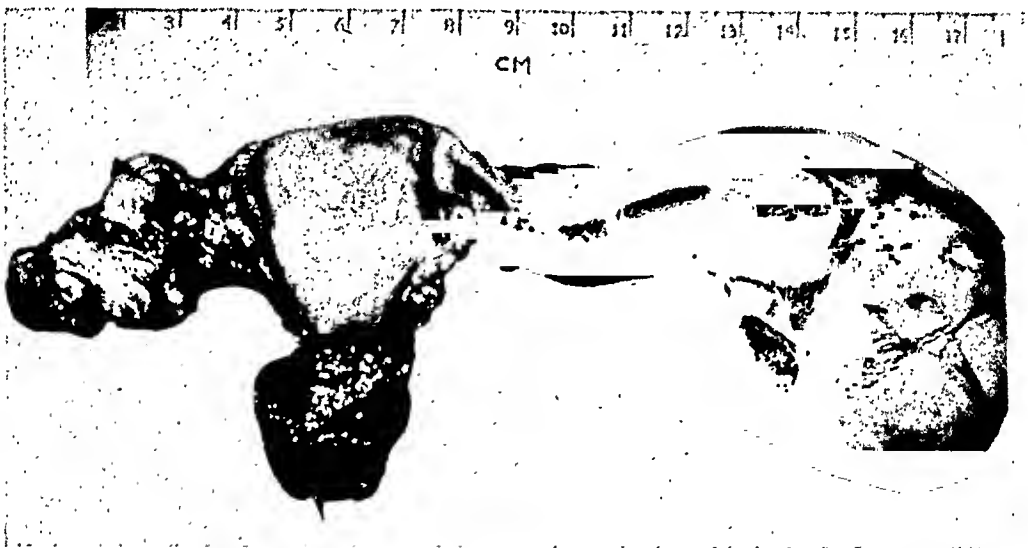


Fig. 2.—Anterior view of removed uterus and adnexa showing sarcoma of left uterine tube and the enlarged right tube. Both ovaries adherent. Uterus atrophic.

The pathologic report, submitted by Doctors Jacob Hoffman, Carl Bucher, and Peter Herbut, was as follows:

*Uterus:* This consisted of a very small normally shaped organ which measured  $6\frac{1}{2}$  by 4 by 3 cm. It was covered by a pink smooth serosa. The uterine cavity measured 4 cm., and was lined by a very thin mucosa. The myometrium measured only  $1\frac{1}{2}$  cm. in width. The cervical canal measured  $2\frac{1}{2}$  cm. in length, and was lined by a thin, slimy mucosa. The portio measured 2 by 2 by  $1\frac{1}{2}$  cm., and was lined by a pink mucosa.

*Right tube:* This organ measured 8 by  $\frac{1}{4}$  cm. and the distal third was adherent to the ovary. Section revealed a narrow lumen. The serosa was partially covered by adhesions.

*Right ovary:* This organ measured 3 by 2 by 1 cm. and was very firm in consistency. Section revealed several corpora albicantes.

*Left tube:* This consisted of a large retort-shaped organ which measured 14 cm. in length. Its diameter varied from  $\frac{1}{2}$  cm. in its inner third to 5 cm. at its most distended portions. The middle and outer third was replaced by a cystic tumor which was translucent to light, and was replaced by a gray friable tissue. The fimbria was sealed. The inner third of the organ was distended with blood, and the wall was very thin.

Receiving other opinions and advice, the patient eventually consulted the senior author on Feb. 29, 1944. Pelvic examination revealed a multiparous outlet with a moderate cystocele and rectocele. The cervix was atrophic and intact. The fundus, however, was thought to be enlarged, boggy, and in retroflexioversion; the adnexal areas could not be distinguished apart from it. When mobilization was attempted, extreme sensitivity was evidenced. A tentative diagnosis of pyometra following irradiation therapy with radium was entertained and surgery recommended if preoperative studies would permit of such a decision.

The advice was accepted and the patient entered Jefferson Hospital on March 6, 1944. She was possibly a substandard risk. Obesity was apparent, her weight being 157 pounds. The vaginal smear (Papanicolaou technique) showed atypical cells, suggestive of fundal carcinoma. The blood count, however, was excellent; urinalysis was negative except for a few leucocytes; bilirubin and bromsulfalein test were normal, as was the blood urea nitrogen, while the urea clearance tests were 38 per cent and 45 per cent on two occasions. The electrocardiogram showed left axis deviation only. Dr. Harold W. Jones, consulting internist, felt that she could undergo major surgery.



Fig. 1.—Section from curettage performed nine months prior to operation showing an atrophic endometrium. Fibrous connective-tissue stroma with a paucity of straight nonsecretory glands. (Hematoxylin and eosin, X50.)

The findings at operation, March 11, 1944, were most interesting. With continuous spinal anesthesia excellent relaxation was obtained, thus permitting a more certain pelvic examination. This disclosed a relatively small, atrophic uterus that seemed to be displaced anteriorly by a more or less fixed but softened enlargement in the cul-de-sac, apparently originating in the left adnexal region and being adherent to the uterus posteriorly. A diagnosis of hydro- or pyosalpinx, secondary to irradiation endometritis, was then made.

No curettage was performed, the cervix being closed with a figure-of-eight suture after carrying out vaginal antisepsis. The abdomen was now opened by a low midline incision. Few adhesions were encountered, and the pelvis was readily exposed. This revealed what appeared to be a relatively large left pyosalpinx, occupying the cul-de-sac and adherent to a small atrophic uterus, displaced anteriorly. The left ovary was atrophic and adherent, and partial torsion of the tubo-ovarian enlargement was apparent. It was mottled, purplish, and congested in appearance. The right tube was hyperemic and swollen, the right ovary being atrophic and adherent, while the entire right

*Ovaries:* Sections revealed several corpora albicans and a poorly vascularized and fibrotic ovarian stroma. There was no evidence of metastatic lesions in either.

*Left tube:* The distal part of the tube was represented by a dilated lumen, a very thin wall, and atrophic plicae. The inner third was distended with blood and was thin walled.

The middle and outer thirds of the tube were replaced by a tumor growth. This was composed of a very cellular and bizarre growth made up of muscle cells and some fibroblasts. The cells showed a marked disparity in size, and clumping of cells were seen throughout. The tubal architecture was entirely destroyed by this malignant connective tissue growth, of intertwining bundles of spindle and round cells, with giant cells.

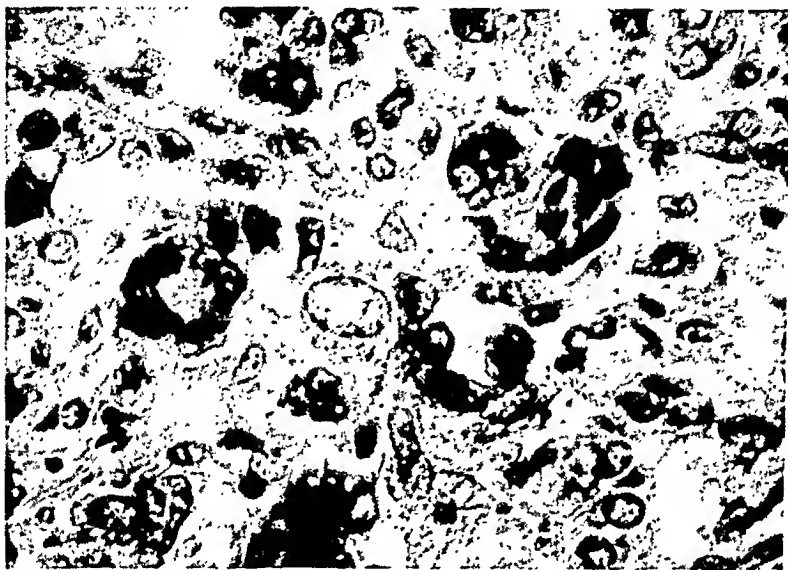


Fig. 5.—Section of the tumor in another area showing extreme pleomorphism with many bizarre single and multinucleated giant cells. (Hematoxylin and eosin,  $\times 400$ ).

*Diagnosis.*—Atrophic endometrium; senile uterus; normal cervix with senile changes; senile changes of both ovaries; senile changes of right tube; and myosarcoma of left tube.

The final diagnosis was myosarcoma of the left uterine tube, and this was a source of astonishment to me and my associates. Slides were sent to Drs. Robert T. Frank and Emil Novak, who confirmed our diagnosis, and their opinions are quoted herewith.

*Dr. Frank:* "After careful study of the section, I do not see any other possible interpretation than that of a myosarcoma, as the tumor cells are visible even where they infiltrate normal muscle."

*Dr. Novak:* "I agree with you entirely as to the pathological diagnosis of sarcoma, an exceedingly rare lesion, as you yourself comment. The growth is apparently of the mixed cell variety, and microscopically shows considerable anaplastic activity in the form of hyperchromatism, mitosis, etc. In addition there are numerous giant cells, often multinucleated. In a few areas the sarcoma cells are arranged in a definitely perivascular fashion, but this is obviously due simply to the better preservation of the cells around the blood channels."

The patient, now 72 years of age, has been seen at regular intervals since operation, is well and active, presenting no evidence of recurrent disease either upon pelvic or general examination.



*Left ovary:* Measured 3 by 2 by 1 cm., and was covered by a rough capsule (wrinkled). Section revealed a homogeneous surface.

*Histology.*—

*Fundus uteri:* The endometrium was markedly atrophic and was merely represented by a single layer of low cuboidal epithelium. The myometrium showed a marked increase in fibrous connective tissue and harbored occluded blood vessels. There was evidence of marked senile change.



Fig. 3.—Section of the tumor from the left Fallopian tube showing a portion of the tubular epithelium surrounded by sarcomatous tissue. (Hematoxylin and eosin,  $\times 50$ .)

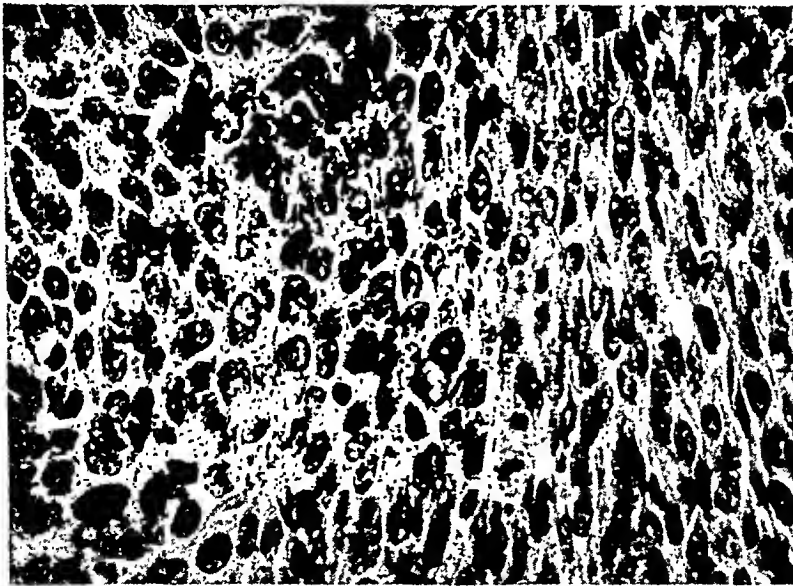


Fig. 4.—Section of the tumor showing intertwining bundles of spindle and round cells. The cytoplasm is moderate in amount and the nuclei are large, deeply stained, but rather uniform. (Hematoxylin and eosin,  $\times 400$ ).

*Cervical tissue:* The portio was lined by an intact stratified squamous epithelium. The underlying stroma was poorly vascularized and showed an increase in fibrous connective tissue. There was no evidence of malignancy.

*Right tube:* The lumen was very narrow. The tubal plicae were markedly atrophic. The muscular and serosal coats appeared normal.



nucleated giant-cell sarcoma. Tubal lumen patent. Fraenkel questioned the diagnosis, but Robert Frank has accepted it. No follow-up.

CASE 12.—1911, *Barbour and Watson*: Aged 53 years, nullipara (bilateral salpingo-oophorectomy). Left tubal perithelioma with local and generalized metastases and ascites. Tubal lumen not patent. Death occurred eleven days postoperatively.

CASE 13.—1915, *Müller*: Bilateral tubal perithelioma. Whether operative or autopsy specimen not mentioned. A simple statement of fact, presented before the Fifth Congress of Czech Scientists and Physicians, in Prague, 1914, stating that during the previous six years only one such case had been found in the Pith Clinic. No details, as the proceedings of the Congress were apparently never published. It is difficult to accept this case without further evidence than that presented.

CASE 14.—1917, *Bello and Castanedo*: Aged 40 years, para viii, operative specimen (salpingo-oophorectomy and supravaginal hysterectomy). Right tubal round-cell sarcoma. Tubal patency not mentioned. Operative recovery. No follow-up.

CASE 15.—1924, *Bannister*: Aged 45 years, para ?, operative specimen (salpingo-oophorectomy and supravaginal hysterectomy). Left tubal small round-cell sarcoma, associated with multiple uterine myomas, and metastatically involved iliac and aortic lymph node. Tubal lumen filled with tumor tissue. Death seventeen days postoperative, possibly from pulmonary embolism.

CASE 16.—1924, *Dodd (I)*: Aged 55 years, nullipara, operative specimen (salpingectomy). Right tubal spindle-cell and "oat-cell" sarcoma. Tubal lumen filled with tumor mass and mucosa destroyed at point of origin. Operative recovery. Well for one year. No further follow-up.

CASE 17.—1924, *Dodd (II)*: Aged 60 years, para II, operative specimen (bilateral salpingo-oophorectomy and appendectomy). Right tubal spindle-cell sarcoma. Tubal mucosa smoothed out. Operative recovery. Death from recurrence and metastases two years later.

CASE 18.—1936, *Bride*: Aged 54 years, para i, operative specimen (bilateral salpingo-oophorectomy and complete hysterectomy). Bilateral tubal perithelioma (perivascular sarcoma). Tubal lumina filled with tumor growth. Operative recovery. No follow-up.

CASE 19.—1938, *Jörgenson*: Aged 62 years, nullipara, operative specimen (salpingectomy). Left tubal giant-cell sarcoma with peritoneal metastases. Tubal patency not mentioned. Postoperative external irradiation. Death forty days postoperative from bronchopneumonia. Autopsy showed no pulmonary metastases.

CASE 20.—1939, *Reiber*: Aged 44 years, para ?, operative specimen (salpingectomy). Right tubal spindle-cell sarcoma. Tubal lumen filled with tumor growth. Operative recovery. Postoperative external irradiation. Well one year later. No further follow-up.

CASE 21.—1945, *Rickford*: Aged 54 years, para iii, operative specimen (salpingo-oophorectomy). Curettage (Aug. 29, 1944) negative. Pelvic operation Mar. 11, 1945. Left tubal spindle-cell sarcoma. Tubal lumen filled with tumor mass, extruding from it and attached to broad ligament and uterus. Operative recovery, with pulmonary infarct sixteen days postoperatively. Postoperative external irradiation. Well seven months later. No further follow-up.

To the above 21 cases designated as sarcomas, is now added the twenty-second case, that of the patient whose case history has been described—a definite myosarcoma of the left uterine tube.

## Chronological Summary of Previously Recorded Cases

CASE 1.—1886, *Senger*: Aged 59 years, para ?, autopsy specimen. Bilateral tubal round-cell sarcoma with pelvic metastases. Tubal patency not mentioned. Had been admitted to hospital and died in diabetic coma. Gebhard questioned the diagnosis, declaring the specimen to be a carcinoma, but Robert Frank and others have accepted it as a sarcoma.

CASE 2.—1886, *Gottschalk*: Aged 37 years, para iii, operative specimen (salpingectomy?). Right tubal small spindle-cell sarcoma with pelvic and lymphatic metastases. Tubal lumen patent. Death occurred four days post-operatively.

CASE 3.—1889, *Janvrin*: Aged ?, para ?, operative specimen (salpingectomy). Tubal myxosarcoma with embryonal connective tissue and unstriated muscle, whether right or left tube not mentioned. Tubal lumen patent. Death after operation, thought to be due to "general nervous exhaustion in the whole alimentary tract" (adynamic ileus? peritonitis, with intestinal obstruction?).

CASE 4.—1890, *Sänger*: Aged 42 years, nullipara; operative specimen (bilateral salpingectomy and resection of left paraovarian cyst). Bilateral tubal small round-cell sarcoma, with left paraovarian cyst in addition. Tubal patency not mentioned. Gebhard questioned this diagnosis also, as did Coe, but other reviewers have accepted it since then. Death occurred eight months later from metastases.

CASES 5 AND 6.—1893, *Jones, C. D.*: In 1890, Prof. H. F. Formad, Coroner's physician of Philadelphia, secured 35 tubal enlargements, supposedly all tubal pregnancies, that were found in women who had died suddenly of intra-abdominal hemorrhage and were autopsied. They were selected from a series of autopsies of over 3,000 adult women, and were submitted to Jones for study. No case histories were available, but three "myelomas of the tube" were described by him—two primary and one probably secondary: (1) large round-cell sarcoma; (2) large spindle-cell sarcoma. (The third was regarded as a secondary melanotic sarcoma.) Tubal patency was not mentioned. He claimed to have traced the gradual transformation of muscle cells into cells of the "myelomata," but this has been disputed. Apart from this interpretation, the illustrations support the microscopic diagnoses of the two primary (and one secondary) tumors, although Von Kahliden and Robert Frank have doubted the acceptance of these cases. Only the primary tumors are recorded in this review.

CASE 7.—1897, *Jacobs (I)*: Aged 41 years, para i, operative specimen (bilateral salpingo-oophorectomy and supravaginal hysterectomy). Left tubal myosarcoma. Tubal patency not mentioned. Death occurred one year later.

CASE 8.—1897, *Von Kahliden*: Aged 51 years, para iii, autopsy specimen. Bilateral tubal endothelioma with giant-cell formation, and metastases to both ovaries and peritoneum. Ascites present. Tumor mass protruded through fimbria of right tube. Robert Frank, contrary to other authors, labels the diagnosis as doubtful, which does not seem reasonable in the light of the present review.

CASE 9.—1904, *Jacobs (II)*: Aged 27 years, nullipara, operative specimen (bilateral salpingo-oophorectomy and supravaginal hysterectomy). Bilateral tubal spindle-cell sarcoma, with ascites and enlarged sacral lymph nodes. Tubal patency not mentioned. Still alive two months later. No further follow-up noted.

CASE 10.—1909, *Gosset*: Aged 44 years, para iii, operative specimen (bilateral salpingo-oophorectomy and supravaginal hysterectomy). Left tubal perithelioma, with metastatic nodules in omentum and broad ligament. Tubal lumen patent. Right hydrosalpinx. Uneventful convalescence, but no further follow-up.

CASE 11.—1911, *Scheffzeck*: Aged 61 years, para ?, operative specimen (curettage and left salpingectomy (?)). Left tubal spindle-cell and multi-

The case presented herewith adds a sixth to those emanating from the United States—all but one having been encountered in Philadelphia. Of the remaining 16, one appeared in Peru, S. A., and the remainder in continental Europe and the British Isles.

### Clinical Features

*Age Incidence:* The age incidence in this series coincides closely with that of the fundal carcinoma group, all but two of the patients ranging in age from 40 to 70 years. The youngest were 27 and 37 years of age, respectively; the eldest (our patient) being 70 years. This is also similar to the age incidence in tubal carcinoma.

*Symptomatology.*—A critical review of the symptoms exhibited by the patients in the series collected shows that the manifestations of tubal sarcoma mimic those described in carcinoma of the tube, the commoner malignant lesion. This is easily understood when the lesions described are viewed in the light of the histologic picture presented, for it has been shown that controversies have repeatedly arisen with respect to the microscopic diagnosis and its similarity to epithelial malignancy. Unfortunately, not all of the histories reviewed are well detailed.

Practically all of the patients were in the premenopausal or postmenopausal epochs. Among the former, menorrhagia and/or metrorrhagia were mentioned, and not infrequently an abnormal vaginal discharge in addition, either serosanguineous or semipurulent. In the postmenopausal group, the discharge was generally described as bloody, but was occasionally of a profuse, watery nature. In the two younger patients (27 and 37 years of age) the menses were normal.

In nearly every case, pain was a prominent symptom. This varied in intensity and duration, being distinctly pelvic in some, diffusely abdominal in others. Often pain went hand-in-hand with gastrointestinal symptoms, such as nausea and diarrhea, together with abnormal bleeding and discharge. Abdominal distention, the sensation of having an abdominal enlargement, pronounced malaise, loss of weight, and even emaciation were sequential to a late advancing lesion with extension or metastases, a train of symptoms observed in about one-third of the patients.

Symptoms such as those recounted may be encountered in any type of adnexal malignancy, either tubal or ovarian, except that the latter may also occur in women of a relatively younger age group.

*Pelvic Examination and Diagnosis.*—Abdominal and pelvic findings varied with the extent of disease present. Abdominal distention or enlargement were noted in five patients, emaciation or cachexia in eight. In most instances pelvic enlargements were discernible, amounting in several instances to a so-called "frozen pelvis." Comparative descriptions varied in size from a "walnut" to a "grapefruit."

In no case was the diagnosis of tubal malignancy entertained preoperatively. Actually, a preoperative diagnosis of any sort was mentioned but 10 times among the 17 operative cases. The diagnoses prior to operation were:

### Pathologic Features

Of the 22 cases now referred to, 17 of the specimens were secured by operation and four by autopsy; in one the source was not mentioned.

Seventeen have been described as sarcomas of various types, involving the wall, the mucosa and the lumen. They are subdivided as follows: nine spindle-cell, large and small; four round-cell, large and small; two myosarcoma, one each as giant-cell sarcoma and myxosarcoma, respectively. Of the remaining five, three have been described as peritheliomas, one as endothelioma, and one as periendothelioma. They are included in this series, for although the exact histogenic interpretation is not too clearly understood, and is to some extent controversial, the consensus of opinion of numerous authors seems to be that all of them should be regarded as sarcomatous tumors (Ewing, Boyd, McCallum, Karsner). There is nothing to indicate what actually initiates the development of a tubal sarcoma.

It has been thought better not to include a small group of closely-related tubal malignancies in the listing of reported cases. These consist of: (1) Seven malignant mixed tumors classified in general as "carcinosarcomas," with certain histologic modifications in two of them. (von Franque, Snger, Schafer, H. R. Spencer, Amann, Motta, Leuret.) (2) A case described as a "mesothelioma" (Egglinton) and one spoken of as a "coelomic mesothelioma" (Collilas and Masciottra). Because of their histologic similarity to true epithelium, these lesions are probably better classified as carcinomas.

The above compilation of the 22 cases now reported provides interesting comment. As noted, seven of the 21 previously reported cases have been subjected to criticism by others.

Thus Gebhard questioned both the cases of Senger and Snger, but this is not surprising in view of the fact that these cases, together with those of Gottschalk and Janvrin, were the first tubal sarcomas to be recorded. Naturally, their interpretation would be subject to minute criticism as new pathologic entities. Dietrich regarded the lesion as a mixed one—sarcoma and carcinoma.

The cases reported by Jones may have been doubted by Von Kahlden, and more recently by Robert Frank, perhaps because of the bizarre theory of tumor development that Jones stressed, rather than upon the histologic picture presented. Our feeling, however, based on a careful perusal of the original article and its illustrations, is that these cases are entitled to inclusion in the series. Our opinion is the same with respect to Von Kahlden's case, accepted by all reviewers with the possible exception of Robert Frank.

Fraenkel disputed Scheffzeck's case on the basis of a comparative study with a certain group of tubal carcinomas of his own, in which he pointed out distinct histologic similarity between them, but Robert Frank and others include the case in reviews of the subject.

With respect to Mller's case, our estimate is that the recorded reference is too brief for certain analysis, but that it should be mentioned in the series as a reported instance of tubal sarcoma.

As stated by Auspach before this Society in 1930, and by others as well, malignancy of the tube is more likely to occur in the late reproductive, menopausal, or postmenopausal periods of life. Vaginal bleeding is not nearly as well-marked as in uterine carcinoma; this symptom is much more likely to be in the nature of a watery, blood-tinged discharge. Pain is probably the most constant and conspicuous symptom, often associated with gastrointestinal annoyance.

The physical signs may be regarded as early and late. In the former, the presence of an adnexal mass (or masses) is about all that one can expect to find. With the advance of the lesion, abdominal distention, ascites, and an extensive pelvic mass are found naturally, while emaciation and cachexia accompany these.

Taking into account the symptoms and signs as mentioned, it is obvious that certain truths evolve with respect to diagnosis. Knowing the clinical manifestations to be what they are, early diagnosis, as in malignancy elsewhere, is the goal to be aimed at. The popularity of diagnostic curettage affords ample opportunity to think of tubal carcinoma or sarcoma when the procedure is negative and especially in the presence of adnexal enlargement. In one of the recorded cases, curettage was negative seven months prior to the laparotomy that disclosed an extending tubal sarcoma. In our own case, curettage and a radium application preceded operation by nine months, due to no fault of the primary operator who advised prompt retreatment. In one of the other cases there had been a curettage immediately preceding the laparotomy.

The physical status of the patient often determines the ease of detecting pelvic pathology. In the lean person, it is not nearly as difficult to carefully follow the patient in whom a tubal lesion is thought of or suspected as it is in the obese individual. Hence, in the latter, examination under anesthesia, with preparations made for immediate abdominal operation if a definite adnexal mass is found, is the procedure of choice.

Once operation is decided upon, the procedure should be complete abdominal hysterectomy with bilateral salpingo-oophorectomy, rather than simple removal of the affected tube and/or ovary. Of course this is not always possible, as has been learned from the cases reviewed. Postoperative irradiation therapy is indicated when operation has been incomplete, either intentionally or of necessity, and the diagnosis of malignancy has been made in the laboratory; likewise when metastases are observed. The question of irradiation therapy when operation has been complete, and where no metastases are visible, is debatable. A large proportion of the recorded cases that were operated upon occurred in the days when x-ray therapy was unknown or in its infancy, and criticism from that source is unjustified. It should be apparent, too, that the gross differentiation between sarcoma and carcinoma of the tube is impossible; in fact a benign lesion of the tube might well be diagnosed visually, as happened in our case.

Finally, it is evident that the prognosis of tubal sarcoma, as well as tubal carcinoma, is doubtful at best. Curability can only be enhanced by early diag-

ovarian carcinoma, two; pelvic inflammatory disease, two; ovarian cyst and pelvic inflammatory disease, one; uterine fibroids, two; tuberculosis, one; "enlargement springing from uterus," one; pyosalpinx or hydrosalpinx following intrauterine irradiation (our case).

*Operative and Autopsy Findings.*—Bilateral tumors were reported in six cases; left-sided in eight, right-sided in five. In three the site was not mentioned. Patency of the tubal lumen was observed six times, is not mentioned in nine cases, while in the remainder the growth extended to, and filled the tubal lumen with extrusion from the fimbriated extremity in some instances. The diameter of the tubal enlargements varied in general from 2 to 20 cm. The appearance was equally variable, depending upon the extent of the lesion and its environment. Usually the tube or tubes involved were distended, of varying shape and consistency, being either solid, soft, cystic, or at times papillary. No predominant coloring was noted, but whenever extrusion of the tumor mass was mentioned, it was described sometimes as being "white and brain-like" in appearance, or "cauliflower-like." Adhesions and/or metastatic growths were present in the majority of cases. Accompanying lesions of adjacent pelvic organs were relatively infrequent.

*Treatment.*—The operative procedures in 17 patients were: salpingo-oophorectomy or salpingectomy, either unilateral or bilateral, 10; with accompanying supravaginal hysterectomy, 5; with complete abdominal hysterectomy, 2 (including our case). In one instance a negative curettage had been carried out seven months before the abdominal operation was performed; in our case, nine months before, with intrauterine radium as well. Postoperative x-ray was employed twice in recent years (1938-1939).

*Results:* Nine operative recoveries, of whom four were living and well two to twelve months after operation, when the cases were reported; one has survived for two years, and is apparently well and free of recurrence (our patient). No follow-up record is noted in the remaining four reported operative recoveries.

Five postoperative deaths occurred (four to forty days); three remote deaths occurred from metastases.

Four of the cases in the series, as noted, were autopsy reports (Senger, Von Kahliden, Jones<sup>2</sup>). Whether it was an autopsy or operative specimen is not mentioned in one case (Müller).

### Summary and Discussion

Our reasons for presenting this communication are twofold. First, to record an unusual pathologic entity, and to review the literature to date with respect to it; second, to discuss the symptomatology, physical findings, and the difficulties encountered in arriving at an accurate preoperative diagnosis.

The first objective has been accomplished, as noted.

With respect to the second, it has been seen that the symptomatology is no wise distinctive, but is akin to that of tubal carcinoma or to ovarian carcinoma in some forms.

an escape of blood from the tube into the uterus? That is the probable explanation, but a most unusual phenomenon.

Third, as time goes on, all of us use intrauterine radium less frequently as a panacea in the treatment of inadequately explained postmenopausal bleeding. Dr. Scheffey's patient is a case in point. Her clinical picture was obscured, in part at least because she had been given radium; and surgery was long delayed because it was thought that her symptoms were the result of local reaction, or infection, incident to the intrauterine radium irradiation.

DR. SCHEFFEY (Closing).—With regard to Dr. Gardner's question as to the primary symptom in this patient, it was apparently a minor hemorrhage. I do not know about the actual amount of blood lost, but it was sufficient to cause her to go to her physician who very rightly performed a diagnostic curettage and applied radium as seemed indicated. It was no fault of his that the patient did not have re-treatment sooner, for she demurred for some time thereafter and sought various opinions.

I would like to emphasize again that it is in the case of the stout patient in whom menopausal and postmenopausal bleeding occurs that we are prone to rely often on diagnostic curettage and a radium application, instead of being prepared to perform abdominal section.

nosis and prompt treatment. The latter, in the final analysis, can be made possible only by a keen appreciation of the symptoms and findings that have been stressed, but more probably by the periodical pelvic examination of women through continued lay and professional education.

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### Discussion

DR. GEORGE H. GARDNER, Chicago, Ill.—First, including the case which Dr. Scheffey has reported, there are 22 more or less authentic instances of primary sarcoma of the Fallopian tube recorded in the world's literature. In other words, only 4 per cent of all malignant tumors of the tubes are sarcomas. Despite their rarity, I shall be much surprised if someone does not report an additional case very soon.

Second, Dr. Scheffey has failed to comment on the mechanism of the postmenopausal bleeding which brought his patient to her physician. I hope he will elucidate. Was it



TABLE I.

RACE	NUMBER TESTED	PER CENT POSITIVE REACTIONS	PER CENT NEGATIVE REACTIONS	INCIDENCE OF ERYTHROBLASTOSIS FETALIS (PER CENT)
White	334	85.0	15.0	2.1
Negro	264	95.5	4.5	0.7
Chinese	150	99.3	0.7	Very rare
Japanese	150	98.0	2.0	Very rare

The small group of 10 per cent will be considered later. The disease rarely manifests itself in the first pregnancy, and, when it does, there is practically always a history of one or more transfusions, the donor or donors being known to be Rh positive, or presumed to be so. Rh testing before transfusion is of course a new development, and with 85 per cent of our white population being in the Rh-positive group, the Rh-negative person being transfused has had only a slight chance of receiving Rh-negative blood. Levine<sup>10</sup> believes that, where hemolytic disease of the newborn is found in the first infant of an Rh-negative woman who has never been transfused, the intramuscular injection of blood to the mother in infancy or in early childhood may have initiated the iso-immunization.

The course of events appears to be as follows: The Rh-positive blood of the fetus (the factor is in the red cells) in some manner crosses the placental barrier. Of course, it has been known for years that fragments of the villi break off and are transported by the maternal blood stream to various parts of the mother's body, particularly the lungs.

Levine<sup>8</sup> believes that these slight lesions might suffice for the entrance of fetal blood into the maternal blood stream, or that other microscopic solutions of continuity might occur. He estimates that only 0.13 c.c. of Rh-positive fetal blood is needed to produce iso-immunization in the Rh-negative mother. Once this occurs, anti-Rh agglutinins are formed, which pass back across the placental barrier to the fetus, produce destruction of the Rh-positive red cells (carrying the Rh factor), with consequent overstimulation of the hemopoietic organs, and a resultant outpouring of immature red cells.

This process is a slow one, so that it can be stated that the first born child of an Rh-negative woman and an Rh-positive man is almost never affected in this manner. The second one usually manifests hemolytic disease of varying intensity, but at times this does not develop until the third or even a later pregnancy. The fetus, as a rule, is not affected until late in pregnancy. It may die in the uterus days or weeks before delivery, or may die even after birth, or may recover if the disease is not of too severe a type and proper treatment is instituted at once. Rarely is abortion caused, as the titer of antibodies in the maternal blood is usually rather low early in pregnancy, and tends to rise as gestation advances. Once the state of iso-immunization is produced, it appears to persist for the lifetime of the woman (Levine<sup>11</sup>).

Iso-immunization of the Rh-negative woman has also been produced many times by the transfusion of Rh-positive blood, especially if repeated.

In a study of 700 Rh-negative women pregnant for the first time, Moller, Levine and Yarrow<sup>12</sup> found 28 cases of hemolytic disease of the newborn. In

## SOME CLINICAL ASPECTS OF THE Rh FACTOR IN OBSTETRICS\*

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THE discovery of the Rh factor is a recent one, it having been first detected by Landsteiner and Wiener<sup>1</sup> in 1940. Levine and Stetson<sup>2</sup> and others had previously suspected the presence of some such substance in the blood. So great is the importance of this factor, both scientifically and clinically, that a voluminous literature has developed. It is impossible to review, in this presentation, the hundreds of papers that have been written. Furthermore, the serologic ramifications are so perplexing that it is best to avoid the controversial aspects of the subject and to confine ourselves to a consideration of the clinical implications.

However, a brief review of the fundamental principles is necessary. It is known that the Rh factor is not a single entity, but a complex one, which helps to explain some of the varying clinical manifestations. Wiener and others have shown that about 85 per cent of white people are Rh positive, with a much greater proportion in other races (Table I from Levine).

Of the 15 per cent negative individuals in the white race, we would expect less than half to be females of the childbearing age. However, Halperin, Jacobi, and Dubin<sup>3</sup> found 66 Rh-negative women in 500 consecutive determinations in pregnant patients (13.2 per cent). Levine, Katzin, and Burnham<sup>4</sup> state that in about 9 to 10 per cent of marriages in the white race, there is the union of an Rh-negative woman and an Rh-positive man.

It is generally thought that in about only 5 per cent of such unions will the baby be affected, and this complication is very rarely seen in the first pregnancy. Buxton and McDuff<sup>5</sup> found 66 cases of erythroblastosis fetalis in 28,898 deliveries, an incidence of 1 to 516. Javert<sup>6</sup> gives a figure of 1 in 438, while Wolf and Negus<sup>7</sup> found their ratio to be 1 in 568. Thus, we can expect an affected infant in about 1 to 500 deliveries. Levine and Waller<sup>8</sup> state that 1 in 150 to 200 newborn children have erythroblastosis, but that about only one in 438 develop clinical manifestations of the disease.

The chief point of clinical interest is this occasional delivery of an infant in whom erythroblastosis fetalis is already present or develops shortly after birth. Wiener<sup>9</sup> proposes the more appropriate designation of "hemolytic disease of the newborn." This occurs in three forms, the anemic, the icteric, and the hydropic types. The mortality is about 55 to 60 per cent, the prognosis being gravest in the hydrops type, and best in the anemic type. Of great clinical importance also is the occasional transfusion reaction following the administration of Rh-positive blood to an Rh-negative recipient, noted more particularly in the last of a series of repeated transfusions.

In approximately 90 per cent of all cases of hemolytic disease of the newborn the mother is Rh negative and the father and the infant are Rh positive.

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testing sera are available. If the wife is found to be Rh negative, it is proper to test the husband also. In this small series of cases (122) under the care of the senior author, it is interesting to note that in four instances the husband was found to be Rh negative also. Of these, three women were multiparas, and, of course, the children already born were found to be Rh negative as well. The fourth woman is a primipara not yet delivered. Hence, there was no possibility of iso-immunization in the present pregnancy. In another multipara the wife was positive and the husband negative. A healthy child was delivered. In the Rh-negative primigravidas with no history of previous transfusion there is no cause for worry, but tests for antibodies are proper, unless we can rule out the possibility of the intramuscular injection of blood in the infancy of these mothers. In the multigravida, tests for agglutinins and blocking antibodies are necessary, and these should be repeated at intervals during the pregnancy, and the titer should be determined when antibodies are found. Wiener's<sup>16</sup> conglutination test should also be routinely employed in the test for Rh antibodies, and we have so used it since its discovery in 1945.

In this connection, it must be noted that investigators were puzzled by finding that anti-Rh antibodies were not detected in as high a percentage of established cases of erythroblastosis fetalis as was expected. This was clarified by the discovery by Wiener<sup>17</sup> of what he calls the blocking antibody, which was also discovered independently by Race and Taylor<sup>18</sup> and named by them the incomplete antibody. Wiener described this as follows: "In addition to the Rh antibodies that produce hemagglutination there are others able to combine specifically with Rh positive cells without producing a visible reaction. If Rh positive blood is mixed with serum containing antibodies of the other type, the blood is not agglutinated by anti Rh agglutinating sera, presumably because all the combining sites on the erythrocytes have been occupied. This type is called the blocking antibody." Hence, testing for these antibodies is also essential in the study of the Rh-negative pregnant woman, especially if she is a multipara, unless the husband is also Rh negative. It appears to us that the presence of the blocking antibody gives a graver prognosis than the presence of agglutinins alone.

Fortunately, it happens that about 50 per cent (49 per cent, Levine) of the Rh-positive husbands of these Rh-negative women are heterozygous. If he should be so in a given instance, there is a 50 per cent chance that the fetus will be Rh negative, and hence will not be affected. However, the husband's status cannot be determined, except by testing with the very rare anti Hr serum, which is not available for routine use. Therefore, we have to draw upon the clinical history for aid in determining this point. Naturally, the history will not aid us unless there have been several pregnancies. This information has been available in only two of our cases (Cases 3 and 4).

As stated above, 122 patients from the senior author's practice are reported here (Table I). Of these, 47 were primigravida, of whom 40 were Rh positive and seven were Rh negative. Of these Rh-negative women, one has been delivered of a healthy normal baby, and six are undelivered. Seventy-five were

TABLE II.

	DELIVERED	UNDELIVERED
Primigravida		
Positive	4 (1 misc.)	36
Negative	1	6
Multigravida	13	46
Positive	7	9
Negative	25	97

19 of these, there was a history of one or more transfusions of the mother, the intervals being as great as eight to ten years. It was possible to check some of the donors, and all were found to be Rh positive. In these patients, the iso-immunization was particularly pronounced; the child was mildly affected in only one case, six were seriously ill, and fetal death occurred twelve times. In the other nine patients (with no history of transfusion), the disease was much milder. There was only one fetal death. Levine and Waller<sup>8</sup> feel that the immunization of these mothers might have been caused by the intramuscular injection of blood years before. We have studied two patients (one in the senior author's practice) who were iso-immunized by transfusion four and nine years, respectively, before the first pregnancies. One delivered a still-born baby, and has since lost a second child (Case 1\*). In the other case, the first infant died forty-eight hours after delivery. She has subsequently lost a second baby, dead in utero (Case 2).

As stated above, 90 to 92 per cent of infants with hemolytic disease are born to Rh-negative women with Rh-positive husbands. The others may be due to iso-immunization due to Rh subtypes, or to the A, O, and B blood factors, or to the very rare Hr factor. A case illustrative of the first possibility was reported by Moller, Levine, and Yarrow.<sup>12</sup> The mother was Rh positive, subtype Rh<sub>2</sub>, while the father and the infant were Rh positive, subtype Rh<sub>1</sub>. Wiener<sup>21</sup> reports an instance in which the mother was Rh positive, subtype Rh<sup>1</sup>; the father and the infant were Rh positive, subtype Rh<sub>1</sub>, Rh<sub>2</sub>. Polayes<sup>13</sup> reports two cases which seemed to be due to iso-immunization of the mothers with the A antigen of the babies. Tilden and Chang<sup>14</sup>, from Hawaii, report an infant with hemolytic disease, with both parents Rh positive and no iso-agglutinins found in the mother's blood after delivery. In three of four other cases observed by the authors, both parents were Rh positive. These could probably be explained on the basis of the Rh subtypes. Davenport (junior author) has studied a case in which the mother was Rh positive, subtype Rh<sup>1</sup>, and the father and the affected infant were Rh<sub>1</sub>. The iso-immunization was apparently caused by transfusion from the husband after the second delivery (no reaction). A second transfusion at this time was also free from reaction (another donor), but a third transfusion from a third donor was followed by a chill and fever. In the next pregnancy (1945) the infant showed a mild erythroblastotic anemia with slight jaundice two days after delivery. The baby recovered without transfusion. In another case of Davenport, the erythroblastosis (second child) was apparently due to incompatibility of major blood groups between husband and wife. The father and the baby were Rh positive, Group B, and mother was Rh positive, Group O. There was no evidence of anti-Rh or anti-Hr antibodies. However, her anti-A titer was 1:128 (normal limits) while her anti-B titer was 1:2048, so that there was a very definite specific increase in the latter titer.

Diamond<sup>15</sup> states that "Erythroblastosis fetalis may develop in infants who do not have hemolytic anemia due to Rh incompatibility, especially those with infection, with congenital malformation of the heart, with anoxia due to atelectasis of the lungs and with intracranial hemorrhage, and even extremely premature infants." Finally, as mentioned by Levine, and Waller<sup>8</sup> in some of these infants there is reason to believe that the diagnosis was erroneous.

From the clinical point of view, it seems that it is wise to test all obstetric patients for the Rh factor, particularly as the possibility of transfusion is always present. The use of what is known as the 85 per cent serum seems to be the practical procedure, reserving the search for the rare subtypes for special cases, and this can be done only by those serologists to whom these particular

\*Details at end of article.

Fourth pregnancy, 1936; term pregnancy, baby weighing five and three-quarter pounds, two transfusions received from father. Child is living, and is Rh negative.

Fifth pregnancy, 1941; term delivery. Intrauterine death two or three days before delivery. No autopsy.

Sixth pregnancy, 1942; baby was slightly premature, weighed five and one-quarter pounds, had no jaundice. Child is living, and is Rh negative.

Seventh pregnancy; due September, 1946. On March 12, 1946, the mother's serum showed no antibodies. On May 22, 1946, conglutination test was positive 1:128, blocking test positive, 1:64. Prognosis for successful outcome of this pregnancy was not so favorable. Section was performed at eight months. Baby survived.

Husband is heterozygous (Rh Rh).

CASE 4.—Mrs. R. D. C. Her first pregnancy occurred in 1940, and ended in a miscarriage at two months. A normal child was born in June, 1941. During next pregnancy her basal metabolism rate was +11, last menstrual period was June 8, 1945. Delivered March 15, 1946 of a healthy girl. Husband, Rh positive; first child, Rh negative, wife Rh negative. No evidence of iso-immunization. Husband is hence heterozygous.

CASE 5.—Mrs. F. was never transfused. Her first child was born in 1942 at term, healthy. Second child was born in 1944 at term; had been dead in utero four days. Autopsy: erythroblastosis. Patient, Rh negative; husband Rh, positive; son, Rh positive. One year later patient's sera still contained blocking antibody and agglutinins.

CASE 6.—Mrs. O. H. In 1943 and 1944 she had term deliveries, resulting in normal children. In 1945 she had a term delivery with a living child. At ten days, the baby became pale and slightly icteric. It was transfused with Rh-negative blood, and lived. Husband is Rh positive; three children are Rh positive; wife is Rh negative. Serum shows anti Rh agglutinins and blocking antibody. Husband is probably homozygous. Will next baby survive?

CASE 7.—Mrs. H. F. experienced three miscarriages at three months; then one at five months; then a full-term normal child, now four years old; then two more miscarriages at three and one-half months. Operated upon for tubal pregnancy in 1938. During next pregnancy her basal metabolism rate was + 22. Last menstrual period had been Dec. 3, 1944. Mrs. F., Rh negative; husband and child, Rh positive. No agglutinins or blocking antibody on May 8, 1945, and on Aug. 2, 1945. Premature delivery of twins occurred Aug. 5, 1945, both lived. Rh factor did not affect pregnancy.

CASE 8.—Mrs. L. F. Miscarriage occurred at six months in 1942. History of hypothyroidism. No history of blood transfusion. Rh type of first husband not known. Remarried in October, 1944. During next pregnancy her last menstrual period occurred Oct. 4, 1945. Wife, Rh negative; husband Rh negative. Rh factor no complication of her pregnancy. She was taking 2 grains desiccated thyroid daily. A term delivery with a normal child resulted.

CASE 9.—Mrs. J. P. E. Jr. Patient was never transfused. First child, three years old. Second delivery, February, 1946 resulted in a healthy child. Husband, wife, and first child all Rh negative, no sensitization possible.

CASE 10.—M. R., a Negro woman, had a term delivery in 1944, resulting in a normal child. Patient was transfused from bank blood. In 1946, delivery of an erythroblastosis (hydropic) child, died at birth. Husband, Rh positive; first child, Rh positive; mother, Rh negative. Mother's blood showed agglutinins and blocking antibodies present. Husband probably homozygous.

multigravidas, of whom 59 were Rh positive and 16 were Rh negative. Of these Rh negative, seven have been delivered, and nine are still undelivered. Three of the Rh negative women have delivered erythroblastotic infants. Mrs. F.'s first child was healthy, the second died in utero several days before delivery; erythroblastosis was seen at autopsy (case 5). Mrs. V.'s (Case 3) fifth child died in utero two days before delivery. She has since had a healthy child, and is now pregnant again, with no agglutinins or blocking antibodies in her blood on March 1, 1946. However, on May 20, 1946 (Case 3), antibodies were found so that prognosis for the present pregnancy is not very good. Mrs. DeB. (Case 1) was evidently iso-immunized by repeated transfusions in 1940; her first child died in utero (erythroblastosis at autopsy), and her second died of erythroblastosis three days after section at the eighth month. Of the four Rh-negative multiparas with Rh-negative husbands, two have delivered normal healthy children, and two are undelivered.

In these 122 cases, the percentage of positive and negative cases does not, of course, represent the true proportions that would be found in a large consecutive series. Besides the patients commented on above, we have selected others not included in this series of 122 for special consideration. These will be referred to later.

It might be mentioned that the majority of these tests were made by most excellent clinical pathologists. The Rh-negative patients were retested by the junior author, and, of these, five were found to be Rh positive, and are listed as such. It is hard to explain this discrepancy, unless it be on the basis of difference of sera, or delay in testing, or difference in potency of the sera. We might also note that, once in this series and once in another case, false positives were obtained due to bacterial contamination of the testing sera or to a technical error. Hence, meticulous attention to details is essential. It is also essential for accuracy to use at least two sera of the same specificity but of different lots, both of which should be frequently tested against Rh-positive and Rh-negative control bloods. As Levine<sup>21</sup> points out, the human testing sera are preferred to the experimental sera secured from laboratory animals.

### Case Reports

CASE 1.—Mrs. DeB. had had an operation for ruptured appendix in 1940, and was transfused. Donor not available at present for checking. Delivery of stillborn macerated child (first pregnancy) in 1944. Reported Rh positive (error) in January, 1945. Pregnant in April, 1945. Found to be Rh negative and iso-immunized. Husband found to be Rh positive. Section was performed one month before estimated date of confinement. Baby was living, weighed 5 pounds, developed icteric type, and died in three days.

CASE 2.—Mrs. E. H., aged 21 years, was transfused at 12 years of age; uncle was donor, Group A, Rh positive. No reaction. First pregnancy terminated Aug. 29, 1944. Infant markedly jaundiced, died two days later. Autopsy: typical findings of erythroblastosis of the spleen and liver. Mother, Group A, Rh negative, husband Group A, Rh positive. In second pregnancy mother found to be iso-immunized with blocking antibody present. Baby died in uterus before delivery.

CASE 3.—Mrs. V., Rh negative; Mr. V., Rh positive.

First baby, 1930; premature, 6 pounds; living, Rh positive, jaundiced at birth.

Second pregnancy, 1932; miscarriage at three and one-half months.

Third pregnancy, 1934; premature, infant, at seven and one-half months, weighing 4 pounds. Baby lived five days. Cause of death not known.

by transfusion can be avoided, as emphasized repeatedly by Levine, by being certain to transfuse Rh-negative females of whatever age only with compatible Rh-negative blood. Furthermore, it appears that at present nothing can be done to eradicate such sensitization of an Rh-negative woman once it has been established. The termination of pregnancy at seven and one-half or eight months by induction or by cesarean section has been advocated, and successful cases have been reported by Diamond.<sup>15</sup> Immediately after delivery the baby should be transfused with compatible Rh-negative blood. Darrow<sup>19</sup> feels that Rh-positive blood can be used for these infants, but the general opinion is that this is not wise, as the agglutinins present in the baby's serum would probably destroy the transfused Rh-positive cells. As mentioned above, the prognosis for these babies is not very good.

### Conclusions

1. Tests for the Rh factor, as soon as facilities, trained workers, and proper sera are available, should be carried out on all pregnant women.

2. In Rh-negative women, the husbands should be tested also. If the husband is negative, the fetus is bound to be negative, and will not have hemolytic disease of the newborn.

3. In Rh-negative women with Rh-positive husbands, tests for Rh antibodies should be performed. This is imperative in multigravidas and in primigravidas with history of previous transfusion. If none is found on repeated tests, the prognosis for the fetus is good.

4. If antibodies are found, the titer should be determined at frequent intervals during the pregnancy.

5. If the titer is rising as the pregnancy progresses, induction of labor or cesarean section at seven and one-half or eight months might enhance the baby's chances. This question is still in doubt.

6. After delivery, the erythroblastotic infant should be transfused at once (the veins of the umbilical cord can be used) with Rh-negative blood, and this should be repeated as often as indicated.

7. The chances of securing a healthy child in subsequent pregnancies when one or more erythroblastotic children have been delivered is not good, unless the husband be proved to be heterozygous. Then it is about 50 per cent.

8. If the husband is homozygous, the next pregnancy should not occur until several years have elapsed after repeated negative tests for antibodies. Even then, the risk is great, as the reticulo-endothelial system probably retains the sensitization for life.

9. Artificial insemination, as suggested by Potter and Willson<sup>20</sup> and by Levine,<sup>22</sup> might be performed, with due regard for all moral and legal implications.

10. It is imperative that all Rh-negative females requiring transfusion, whatever age, receive only compatible Rh-negative blood.

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CASE 11.—Mrs. A. R. In 1943 a miscarriage occurred at three and one-half months. She was transfused from husband, and experienced urticarial reaction. In 1944, premature delivery of a six and one-half-month fetus occurred, which was grossly normal. No autopsy. In 1945, the patient had a miscarriage at two and one-half months. Tested one month later, husband was Group O, Rh positive; wife was Group O, Rh negative. Iso-agglutinins and blocking antibodies were present. Prognosis for future pregnancy is not good.

CASE 12.—Mrs. S., aged 30 years, had miscarriages in 1937 and 1938. A term delivery occurred in September, 1941, resulting in a normal child. Second delivery was January, 1946; the baby lived three days. Clinical diagnosis was erythroblastosis. No autopsy. In May, 1946, the father was found to be Group O, Rh positive; son, Group B, Rh positive; mother, Group B, Rh negative. Conglutination and blocking test was positive. Prognosis for future pregnancies is very grave.

### Comments

Case of Mrs. DeB. (Case 1). It is very doubtful that this patient will ever be able to have a healthy child, unless by artificial insemination from an Rh-negative donor.

Mrs. E. H. (Case 2). Same comments as in previous case.

Mrs. V. (Case 3). It is probable that this patient can have more healthy children as the husband is heterozygous.

Mrs. R. D. C. (Case 4). We have not yet been able to obtain blood from the second child for a study. If it is negative, the prognosis for next pregnancy is excellent. If it should be positive, there is a possibility of iso-immunization, and the mother's blood should be tested frequently for antibodies.

Mrs. F. (Case 5). The fact that this patient's blood still contains antibodies at the end of a year makes the prognosis for future pregnancies very guarded. It is interesting to note that she is a double first cousin of another Rh-negative woman in this series. This second patient, however was fortunate enough to have married an Rh-negative man, and to have had healthy children. Extensive studies on the parents and siblings of these patients are to be undertaken.

Mrs. O. H. (Case 6). In view of the fact that all three children are Rh positive, it is most probable that the husband is homozygous, and therefore it is probable that succeeding children will be affected with hemolytic disease with increasing severity.

Mrs. H. F. (Case 7). Tests have not been performed on the twins delivered Aug. 5, 1945. This is to be done, as it will help us to determine whether the father is homozygous or heterozygous.

Mrs. M. R. (Case 10). This is the only case of hemolytic disease due to Rh incompatibility found in the Negro, as is to be expected because of the rarity of Rh-negative women in that race. She may have been sensitized by the transfusion or by the previous pregnancy, or by both. Another case has been encountered by the junior author, but it was strongly suspected that this patient has white blood, so she was not included in this study.

Mrs. A. R. (Case 11). The fact that antibodies were found in the patient's blood a month after an early miscarriage makes the prognosis for future pregnancies very unfavorable.

Mrs. S. (Case 12). In this patient, also, antibodies were found four months after delivery of an affected child. Consequently, we also consider the chance of a healthy child in a future pregnancy is not good.

Although this question is more in the province of pediatrics, a few words as to management of Rh-negative patients might be in order. As far as is known, little can be done to prevent sensitization by pregnancy. However, sensitization



# REVIEW OF CASES OF Rh ISO-IMMUNIZATION DURING THE PAST FIVE YEARS IN THE ROYAL VICTORIA MONTREAL MATERNITY HOSPITAL\*†

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SINCE the discovery of the Rh factor,<sup>1</sup> extensive investigations have been carried out by many workers. It has been demonstrated that the Rh factors play a role in the pathogenesis of hemolytic disease of the newborn<sup>2, 3</sup> and in intragroup transfusion reactions.<sup>4</sup> A review of this work is beyond the scope of this paper. For a comprehensive background of the subject, the reader is urged to refer to the excellent recent publications by some of the outstanding authorities in this field of research.<sup>5-8</sup>

Opportunities for the thorough study of Rh iso-immunization as a cause of hemolytic disease of the newborn have been limited by the relative infrequency of this disease. In addition, much has been missed in explaining the mechanism of the disease and its antepartum prognosis because of the existence of two types of Rh antibodies, one of which was demonstrated only recently. These antibodies have been variously named by different authors,<sup>7, 9-11</sup> but we persist in using the terms "agglutinating" and "blocking" antibodies. Most cases are still available for postpartum study and, if these be investigated both from the maternal and fetal point of view, much useful information may be obtained.

It is with such a study that this paper is concerned, namely, a review of the obstetric cases delivered at the Royal Victoria Montreal Maternity Hospital for the five-year period ending Dec. 31, 1945—a total of 12,114 cases. The hospital files for (a) "fetal deaths," (b) "fetal complications discharged alive" and (c) "neonatal blood transfusions," were examined for cases of erythroblastosis, severe jaundice of the newborn, severe anemia of the newborn, hydrops, hemolytic anemia of the newborn, or any other diagnosis which might have been classified under hemolytic disease of the newborn.<sup>12</sup> A total of 37 cases was found, giving us an incidence of clinical diagnosis of hemolytic disease of the newborn in one out of every 327 deliveries.

The relevant information from the case records of these 37 cases was compiled. Home visits were made in all cases which could be traced with the object of examining the child if still alive, checking histories, and obtaining blood from all available members of the family. In those cases where the child survived, it was subjected to a cursory examination to ascertain whether it could be classified in the broad group of normals, or whether it was an obvious subnormal, either physically or mentally. With the blood obtained, the A.B. and

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(For Discussion, see p. 932.)

pneumonia, one twenty-six days post partum, the other three and one-half months. Of the remaining 13 children, 11 were examined, the other 2 were discharged alive from the hospital, could not be traced, but are presumed alive. Of the 11 babies examined, 8 were normal and had not had a greater incidence of morbidity since birth than could be expected from any group of normal children. The remaining 3 cases, however, are markedly retarded mentally, and all have residual spasticity. It is interesting to note that there were no intermediate types, all children examined could, without difficulty, be classified as normal, or very definitely subnormal.

TABLE II. SHOWING DETAILED OUTCOME OF THE 30 CASES OF ASSUMED HEMOLYTIC DISEASE OF THE NEWBORN

YEAR	NO. OF CASES	LIVE-BIRTHS	STILL-BIRTHS	NEO-NATAL DEATHS	LATER DEATHS	DIS-CHARGED ALIVE—NO TRACE	ALIVE TODAY	NORMAL	SUB-NORMAL
1941	3	3	0	0	1	0	2	1	1
1942	4	2	2	0	0	0	2	1	1
1943	9	5	4	2	0	1	2	1	1
1944	6	6	0	2	0	0	4	4	0
1945	8	3	5	0	1	1	1	1	0
	30	19	11	4	2	2	11	8	3

TABLE III. DETAILS OF TREATMENT BY TRANSFUSION

YEAR	NUMBER OF LIVEBIRTHS	NUMBER TRANSFUSED	TRANSFUSED		NOT TRANSFUSED; DIED
			LIVED	DIED	
1941	3	3	3	0	0
1942	2	2	2	0	0
1943	5	4	2	2	1
1944	6	6	6	0	0
1945	3	2	2	0	1
	19	17	15	2	2

Seventeen of the 19 livebirths in the series were treated by repeated blood transfusions (from one to eight). Of this number, 15 were discharged alive from the hospital (Table III). The two cases not receiving transfusions died within the first week post partum. This strongly indicates the necessity of repeated blood transfusions.

It is of interest to consider the presence of maternal Rh antibodies in relation to time post partum (Table IV). Of our 23 cases which were shown to possess antibodies post partum, 13 were exclusively of the "blocking" type, three were of the "agglutinating" type, and seven showed a combination of both.

It will be noted that the "blocking" antibody persists for a longer time, as long as five years in one case, and has a tendency to be of higher titer than the agglutinating type. The average titer of the blocking antibodies of the cases of one year or less is about twice as high as the average of the cases of three years and over, indicating a gradual decline in antibody titer.

It will be seen by consulting Table V, that the incidence of the present cases of hemolytic disease of the newborn occurs with greatest frequency with the second and third pregnancies, and falling off with the fourth and fifth. Of the

O. and Rh types were determined, and Rh or A.B. and O. incompatibility established. The mother's serum was further tested for evidence of iso-immunization.

For Rh typing<sup>13</sup> standard Rh<sub>0</sub> sera obtained from various sources were used. To demonstrate the presence or absence of antibodies, the mother's serum was incubated with serum suspended cells,<sup>14</sup> or was incubated with saline suspensions, washed, and bovine albumin added.<sup>15</sup> In a few cases rabbit anti-human-globulin serum was added to thrice-washed sensitized cells,<sup>7</sup> the mother's serum having been used for the sensitization. All readings were made under the low power of the microscope without removing the cells from the test tube. For all tests the same four group "O" bloods were used, they were of the following types: Rh<sub>1</sub>, Rh<sub>1</sub>Rh<sub>2</sub>, Rh', Rh<sub>2</sub>. Positive and negative control sera were included in each series. When these tests demonstrated the existence of Rh antibodies, the sera were tested in serial dilution against Rh<sub>1</sub> and Rh<sub>2</sub> cells in saline to demonstrate the absence or presence and titer of agglutinating antibody, and in serum suspension for the blocking antibody titer.

TABLE I. DISTRIBUTION ANALYSIS OF THE 37 CASES BY YEARS

YEAR	TOTAL NO. OF CASES	PROVED BY ANTIBODIES	STRONG PRESUMPTIVE EVIDENCE	QUESTIONABLE EVIDENCE
1941	4	1	2	1
1942	5	3	1	1
1943	10	7	2	1
1944	9	5	1	3
1945	9	7	1	1
	37	23	7	7

Before tabulating the results, our first concern was to verify the accuracy of our selection of cases for inclusion under hemolytic disease of the newborn. Of the 37 cases (Table I), 23 were proved by the demonstration of Rh antibodies in the mothers' sera post partum. All these women are Rh negative. There were no definite cases which could be proved on the basis of A.B. and O. incompatibility. Of the remaining 14 cases, seven were considered as hemolytic disease of the newborn on the basis of the presence in the same case of a combination of several of the other diagnostic points; such as the appearance in early neonatal life of jaundice, pallor, edema, splenomegaly, hepatomegaly, hemorrhages, signs of cerebral damage (spasticity), circulating nucleated red blood cells in large numbers, typical placental changes,<sup>16</sup> Rh incompatibility between mother and child without demonstrable antibodies, postmortem pathologic confirmation, and a typical family history. (Two of these cases showed absence of antibodies, the remainder could not be tested.) The remaining seven cases, although showing some of the above diagnostic points, did not have sufficient evidence to justify inclusion as definite cases of hemolytic disease of the newborn. Thus, this study includes only the first 30 cases mentioned above, which gives us a corrected incidence of one case in 404 deliveries, which is a higher incidence than that found in another recent review of a large series of deliveries—56 cases in 28,898 deliveries, or 1 in 516.<sup>17</sup>

Of the 30 selected cases (Table II) 19 were livebirths and 11 were dead-born. Of the livebirths, 4 died within the first week of life; and 2 died of

The mothers in our 30 selected cases had had a total of 84 pregnancies previously, of which 31 resulted in abortions, miscarriages, stillbirths, or neonatal deaths. Eight of these 30 mothers had subsequent pregnancies, of which 6 were stillbirths and 2 livebirths. Both of these children are Rh negative, still alive and well, and, incidentally, represent the number of good children predictable.

From the foregoing information, it becomes obvious that the importance of Rh iso-immunization does not lie in the frequency of its occurrence. The importance lies in the seriousness of its manifestations in an individual so immunized from the point of view of raising a family of healthy children. There is also the danger of hemolytic reactions to blood transfusions, but the importance of this is minimized by the transfusing of Rh-negative individuals with Rh-negative blood. This is especially true relative to Rh-negative women, regardless of their age.

Proper handling of an obstetric patient who has had some mishap due to the Rh factor must be a combined effort. Modern forms of investigation and treatment executed by the obstetrician, pediatrician, serologist, and pathologist should play their useful parts.

However, the obstetrician has the initial contact with the individual patient. He is frequently asked one or several of the following questions: Should a routine Rh-factor determination be done on every obstetric patient? What is the management during pregnancy of the patient who had had previous complications relative to this incompatibility? Is a therapeutic abortion ever indicated? What is the recommendation in regard to future pregnancies? How is the baby treated following delivery?

A brief statement concerning our personal approach to these problems should be made. In recent months, some doctors and many patients are prone to explain the cause of various fetal catastrophes as being due to the Rh factor. Conditions in newborn infants, such as congenital abnormalities, asphyxia, and intracranial hemorrhage are very often wrongly attributed to this incompatibility. Hemolytic disease of the newborn is comparatively infrequent, as this series indicates. Nevertheless, when this complication does occur, the result is frequently most disastrous.

Our present attitude in the Royal Victoria Maternity Hospital is that all obstetric patients are typed with standard Rh<sub>0</sub> agglutinating serum. When a woman is Rh-negative, an attempt is made to determine her husband's type. This is insisted upon if there is a history of any fetal mishap in previous pregnancies. If indicated, Rh-negative women are tested for antibodies at the third, sixth, and eighth months of pregnancy. This is part of a routine blood examination, which also includes red blood cell count, hemoglobin estimation, and serology to exclude syphilis. The fact that the Rh-factor is being tested is not mentioned to the patient, any more than one tells her that a Wassermann examination is being done. Too much emphasis can be put upon this test, especially when the patient is intelligent and fairly conversant with modern news reports.

If antibodies are present in the pregnant individual, the type and titer are determined; the titration is repeated each month. When the strength of the antibody titer increases to a level of 1:100, we take this as indicative of fetal

TABLE IV. SHOWING THE LEVEL OF RH ANTIBODIES IN RELATION TO TIME POST PARTUM

TIME IN MONTHS	AGGLU- TINATING ANTIBODY	BLOCKING ANTIBODY	TIME IN MONTHS	AGGLU- TINATING ANTIBODY	BLOCKING ANTIBODY	TIME IN MONTHS	AGGLU- TINATING ANTIBODY	BLOCKING ANTIBODY
56	0	1:128	25	1:8	1:64	8	1:16	1:128
49	0	1:2	20	0	1:32	8	1:256	1:128
47	0	1:16	18	0	1:4	3	0	1:64
37	1:2	1:32	18	1:16	*--	3	0	1:16
36	1:16	1:16	18	0	1:8	1	0	1:16
36	1:4	1:16	12	0	1:16	1	1:32	*--
34	1:8	1:8	10	0	1:128	(1 day)	1:8	*--
25	0	1:32	8	0	1:16	----	----	----

\*These three cases were done before we adopted the serum dilution method and could not be repeated.

four incidences after the fifth pregnancy, all cases had had previous fetal mis-  
haps dating back to their third and fourth pregnancies. The case occurring in  
the first pregnancy is one of the living spastic mental deficient, who was in-  
cluded in this series in the "presumptive" group. This baby showed generalized  
edema, jaundice, pallor, typical hemogram, and spasticity shortly after birth.  
The mother and father are both Rh positive. But no evidence of Rh subgroup  
iso-immunization could be demonstrated five years after birth; this is one of  
those cases which is typical of hemolytic disease, except for the demonstration  
of iso-immunization. Of the other 29 women, 27 were Rh negative, the other  
two being unknown and classified in the "presumptive" evidence group.

TABLE V. SHOWING THE PREGNANCY IN WHICH OUR 30 SELECTED CASES OCCURRED

PREGNANCY	1ST	2ND	3RD	4TH	5TH	6TH	7TH	8TH	9TH	10TH	11TH
Number of cases	1	9	8	5	3	1	0	0	1	1	1

TABLE VI

	NUMBER OF CASES	LIVEBIRTHS	STILLBIRTHS	ALIVE TODAY
Interrupted at 36 weeks	7	4	3	1
Full-term deliveries	23	15	8	12

Seven of the 30 pregnancies were interrupted at about the thirty-sixth  
week, 5 by cesarean section, and 2 by other methods (Table VI). This resulted  
in 4 livebirths, and 3 stillbirths, which is a higher ratio of stillbirths than that  
occurring in the full-term pregnancies (15 livebirths, 8 stillbirths). Further-  
more, there is only one living child from these 7 interrupted pregnancies. Thus,  
premature interruption has not yielded good results in this series.

Complications during the pregnancies of the 30 selected cases included 4  
cases of varying degree of toxemia, an incidence which is not significantly above  
that found in pregnancies not productive of cases of hemolytic disease.<sup>18</sup> There  
was one case of placenta previa centralis, and one case of painless bleeding in the  
third trimester. There were no other serious complications of pregnancy, in-  
cluding retroplacental hemorrhage. We were particularly on the lookout for  
this latter complication, in view of recent claims of the presence of a significant  
correlation between this condition and Rh iso-immunization.<sup>19</sup>

2. Of these 30 cases there were 19 livebirths: 13 still living, 8 normal, 3 definitely subnormal, and 2 unknown.

3. Rh antibodies were demonstrable in the majority of mothers post partum.

4. Hemolytic disease of the newborn occurred most frequently in the second and third pregnancy.

5. Fetal mishaps were of high incidence in the total number of pregnancies in these mothers.

6. No other complications of pregnancy could be related to Rh iso-immunization.

7. Interruption of pregnancy at the 36th week has not yielded good results.

8. Repeated blood transfusions are recommended in treatment of the babies.

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### Discussion on Papers of Dr. King and Dr. Philpott

DR. BENJAMIN P. WATSON, New York, N. Y.—In the few years which have elapsed since the significance of the Rh factor in relation to fetal and neonatal pathology was brought to our attention, two things have happened. First, the whole subject has become more and more complicated, at least to those of us who are not immunologists. I cannot add anything to the discussion of these newer concepts of the Rh factor, blocking antibodies, desensitization, etc.

Second, with the accumulation of cases, there has come a change in our evaluation of the risks to the child born of an Rh-negative mother and an Rh-positive father. The prognosis is not nearly so bad as we were at first inclined to think. It is this aspect of the subject that I should like to discuss.

In a period of eighteen months, we have had in the Sloane ward service 175 Rh-negative mothers with Rh-positive husbands. From these matings there were only 12 cases of erythroblastosis fetalis, or approximately 7 per cent. In a single year out of 1,700 viable births, there were only five cases of erythroblastosis fetalis, or approximately 0.3 per cent.

We know that the first pregnancy is quite likely to result in a healthy child, unless the mother has had a previous blood transfusion with Rh-positive blood. Out of a total of 30

involvement. This is especially significant if the history denotes previous fetal mishaps. In seven cases, we interrupted the pregnancy at the thirty-sixth week, for the purpose of lessening damage to the fetus.

It has not been our practice to interrupt pregnancy before viability, with the indication being a high antibody titration only. But where the case history denotes repeated fetal mishaps, and with the husband not established as heterozygous, this attitude may be modified. In this last instance it is advisable that the patient should be instructed in contraceptive methods. Even ligation of the tubes should be considered.

In the face of our experience and that of others,<sup>20</sup> prognosis of pregnancies based on antibody studies has not in the past yielded results which justify a dogmatic stand on this particular aspect of the course of the disease. It is hoped that after some information has been accumulated from antepartum antibody studies, particularly with the newer knowledge of the blocking and agglutinating antibodies, we will be able to formulate a more definite course of action.

Analgesia and anesthesia at the time of delivery must be well chosen. Any type which diminishes the oxygen-carrying content of maternal blood should be avoided. Fetal anoxia and atelectasis may be accentuated if this type of case is poorly handled.

Early diagnosis is essential in the adequate treatment of the affected baby. The babies of all our Rh-negative mothers, whether they exhibited antepartum antibodies or not, are typed for the Rh factor immediately after delivery. In this group, daily hemoglobin estimations are done on all Rh-positive babies for the remainder of their stay in hospital.

The photoelectric method is used on blood from the heel. In a recent study by one of us (to be published later), it was found that the average hemoglobin on cord bloods was 106 per cent, while samples from the heel immediately after birth averaged 126 per cent. In this series of normal infants, no case fell below 100 per cent, hence the 90 per cent quoted below does not refer to cord blood which averages 20 per cent lower than heel puncture immediately after birth. If the hemoglobin level is below 90 per cent at birth, or if the daily drop is more rapid than normal, estimations are performed two or three times daily, and these babies are given repeated small transfusions (10 c.c. per lb.) of Rh-negative whole blood as the mainstay of their treatment. Among the supportive measures must be mentioned the interdiction of the mother's milk which has been shown<sup>18, 24</sup> to contain Rh antibodies of high titer in some cases. Transfusions by the exsanguination and total replacement method have not been tried because of technical difficulties and the possible medicolegal complications in case of death. In addition, it is the opinion of many that this procedure is of no greater value than repeated small transfusions. We have not used washed Rh-negative cells for transfusion as yet, but we propose to do so at the next opportunity, in view of the recent theory<sup>8</sup> on the mode of action of the blocking antibodies.

### Summary

1. In 12,114 deliveries at the Royal Victoria Montreal Maternity Hospital, there were 37 cases of hemolytic disease of the newborn, diagnosed clinically, of which 30 cases are considered as proved, an incidence of 1 in 404.



Potter states that in 13,500 of our patients there were 2,026 Rh-negative women (15 per cent) who gave birth to 48 (2.4 per cent) babies with erythroblastosis. The incidence of erythroblastosis was 0.44 per cent in primipara, and 1.2 per cent in women who were in their fourth pregnancy.

There is no relation between anti-Rh agglutinins and abortion, toxemia, or other complications of pregnancy. Several years ago, Potter and I proved to our satisfaction that the injection of 50 to 100 c.c. of Rh-positive blood into two women with Rh antibodies resulted in hemoglobinemia. Since then several deaths due to transfusion nephritis from Rh incompatible blood have been reported. I have not hesitated to give transfusions of Rh-positive blood to Rh-negative patients if the latter were in desperate need of blood but, have simultaneously alkalized the patient with sodium lactate given intravenously.

There is considerable confusion among the serologists about terminology. I think too many have reported prematurely.

Erythroblastosis and the Rh groupings are accepted conditions, but the theories as to etiology are very uncertain. Each new group requires additional propping. I believe careful and well-controlled studies are necessary to determine method of immunization, transfer of agglutinins back to fetus, mode of action on fetal erythrocyte, etc.

The diagnosis of anemia is of importance. The cord hemoglobin ranges from 14 to 20, with an average of 16.5 per cent, and the hematocrit from 46 to 60, with an average of 54 with heparin and 46 with oxalate. The red blood count varies from 4 to 5.5 million, with an average of 4.5. The capillary blood taken within thirty minutes of delivery ranges from 18 to 27, the average being 22 grams per cent hemoglobin, and the red cell 4.8 to 7, with an average of 6.3 millions. In other words, a capillary hemoglobin less than 18 within the first twenty-four hours is indicative of anemia. If the mother is Rh-negative and the fetus is Rh-positive, Rh-negative blood should be given and erythroblastosis should be suspected. If facilities are not available for determining the Rh group, the mother's washed cells may be used for transfusion.

The immature erythrocytes are poor carriers of oxygen and  $\text{CO}_2$ , which may account for the brain damage due to anoxia.

Exsanguination-transfusions have been used in several clinics with some success and should have further trial. We have used this method with success in two babies. Several babies seriously ill from erythroblastosis did not live long enough for us to transfuse, much less to bleed. Intravenous administration of oxygen has been reported as being of value in combating anoxia and should be tried.

DR. LOUIS CARNAC RIVETT, London, England.—I believe that some effort should be made to persuade the hematologists to agree on a uniform nomenclature for all of these subgroups of the Rh factor. I find in each department that they are quite different, and it is hard to correlate them.

Secondly, there is the possibility of the fetal red blood cells passing into the maternal blood to account for these comparatively rare cases where they develop antibodies, as compared with the certainty with which patients develop them if they have had a previous transfusion. It is quite clear that a blood transfusion of such women with Rh-positive blood will always produce an antititer. On investigation, light might be thrown on the contradiction that some Rh-negative women do not produce antibodies during pregnancy.

Dr. Philpott noticed one case where the antibodies had been present for several months. A couple of months ago I operated upon a woman to whose history I had not paid a great deal of attention. She had had two babies; the first, fourteen years ago, was stillborn after a breech delivery. Two years later she had her second pregnancy. It had been a very difficult delivery, with extensive perineal laceration, and the baby died after a few days. Twelve years later I did a repair of the perineum, and on the eighth day she had a slight hemorrhage which was easily controlled. As she was a bit pale, she was given a blood transfusion from which she never recovered. The blood was Rh negative with a very high (1 in 1028) antititer which must have persisted for twelve years.

cases of erythroblastosis in ward, private, and babies' hospital patients, only five occurred in first pregnancies. Three of the mothers had had previous transfusions, and in a fourth the previous history was unknown. It is, therefore, important for the future that no blood transfusions be given to a female child, girl, or woman without prior determination of her Rh status; that only Rh-negative blood be given to the Rh-negative female.

If the mother has had one erythroblastic child, the chances of future successful pregnancies are much diminished, but they are by no means hopeless, even if the husband is homozygous. In illustration I cite two cases.

CASE 1.—A Negro multipara, gravida vii, para v. Her *first* child had a secondary anemia of unknown origin, from which it recovered. Her *second* pregnancy resulted in an erythroblastotic infant that died forty hours after birth, following two transfusions of mother's blood. A *third* pregnancy ended in spontaneous abortion. Her *fourth* child had erythroblastosis, received Rh-negative blood transfusions, but developed sepsis, and died on the eleventh day. A *fifth* pregnancy ended in early abortion. Her *sixth* baby was icteric at birth and had a severe erythroblastotic anemia which responded to Rh-negative blood transfusions. A *seventh* child became jaundiced twelve hours after birth, had a moderately severe erythroblastosis, and recovered after transfusions with Rh-negative blood.

CASE 2.—A white multipara, gravida vi, para vii. Her *first* child was normal. A *second* baby became jaundiced and anemic shortly after birth, but recovered without specific treatment. Her *third* child was also jaundiced and anemic shortly after birth, and also recovered without specific therapy. Her *fourth* and *fifth* babies were jaundiced at birth and died shortly after without specific therapy. Her *sixth* pregnancy resulted in premature erythroblastotic twins, one of whom recovered after Rh-negative blood transfusions, and one of them died despite this therapy.

In some patients no sensitization may occur over a long series of pregnancies, as in a third case I should like to mention.

CASE 3.—This white multipara, gravida xv, was Rh negative and her husband Rh positive (genotype unknown). All her children have been normal, except for term stillbirth in the last two pregnancies; the first was due to complete separation of the placenta; the second followed rupture of the uterus.

It is cases such as these, and others could be cited, which make us less pessimistic than we were formerly, and which influence us in our advice to patients. We do not advocate routine therapeutic abortion in women who have had erythroblastic children if they are anxious to try again. If they have had previous disappointments and do not wish to risk another, the pregnancy may justifiably be terminated.

We do not advocate routine induction of labor or cesarean section before or at term. We make examinations for agglutinins from the sixth month onward, and usually find that they do not appear till after delivery. Babies born alive usually show no jaundice or fall in red cell count for twelve or more hours after birth. They can then be treated by transfusion of Rh-negative blood. We feel that no transfusion should be given till the necessity becomes evident.

If blocking antibodies are present in the mother's blood during the pregnancy, premature termination may be considered in an attempt to save the child. Finally, there is the further hope of the possibility of the development of some method of desensitization.

DR. WILLIAM J. DIECKMANN, Chicago, Ill.—One of the essayists stated that the importance of Rh iso-immunization does not lie in the frequency of its occurrence, but in the seriousness of its manifestation in an immunized individual.

The incidence on our service of Rh-negative pregnant women at the Chicago Lying-in Hospital is 15 per cent, and of erythroblastosis is 0.35 per cent. Only 2.4 per cent of Rh-negative mothers have erythroblastotic babies. Only 8 per cent of our total fetal mortality is due to this condition. The fetal mortality for erythroblastosis is 67 per cent. The question of an increased incidence of feeble-mindedness in Rh-positive children from Rh-negative mothers has been raised. Dr. Philpott reports that at present 25 per cent of their babies who had hemolytic disease of the newborn are mentally retarded. This possibility must be kept in mind.

The blood submitted with this form is tested for the presence or absence of Rh antibodies, and the result of this test reported to the physician. If Rh antibodies are present, the type of antibody and its titer is also reported. The physician submits subsequent blood samples at intervals throughout the patient's pregnancy on a simple form similar to that used for the husband's blood.

This plan is helpful to the physician, because it enables him to know whether he is going to deliver an infant with hemolytic disease of the newborn, and it is helpful to those of us who are interested in the study of the Rh factor, because it has and will give us an abundance of valuable material and information.

A very brief summary of some of our findings are presented in Table I.

TABLE I.

Total deliveries City of Rochester from	4,717	
Oct. 1, 1945, to May 1, 1946		
Prenatal Rh tests	5,567	
Rh-negative tests	690	14.1 per cent
Positive tests for Rh antibodies	20	
	(1 case in every 34 Rh-negative mothers)	
	(1 case in every 278 tests)	
Infants born with hemolytic disease	9	(1 case in every 524 deliveries)
Mortality from hemolytic disease	6	(1 case in every 786 deliveries)

DR. G. D. ROYSTON, St. Louis, Mo.—There are a few points in these presentations that I should like to emphasize. As the other speakers have stressed, it is vitally important to know the Rh blood picture in connection with every woman who is pregnant or likely to be transfused; also, whether or not she has ever had any kind of intravenous or intramuscular blood injection.

Diamond, in an excellent review of the literature published in the *New England Journal of Medicine* in April, 1945, estimated that probably 80 to 90 per cent of the transfusion reactions were due to Rh incompatibility. All blood sent to the laboratory should be tested with anti-Rh serum of the highest possible potency and of wide specificity while the blood is still fresh, preferably within twenty-four hours after being withdrawn.

I fully agree with all points made by Dr. Philpott. Although erythroblastosis is of grave import, yet, despite the mating of Rh-negative mothers with Rh-positive fathers, the incidence of severe forms of the disease is less frequent than stated in many articles. Among more than 5,000 personal deliveries, I can recall less than a dozen instances of fatal erythroblastosis. Probably more cases of the milder form, as congenital anemia, occurred and recovered without receiving any special treatment.

In the Rh-negative mother and the Rh-positive father, we check the mother's blood at frequent intervals from the thirty-second week of gestation onward, and, if antibodies are found, we deliver the patient after the thirty-sixth week and give immediate blood transfusions of 60 c.c. every one or two days (oftener in the more severe cases) until the child is out of danger.

We feel that delivery earlier than thirty-six weeks' gestation increases infant mortality from prematurity. We also feel that if transfusion is delayed until after symptoms appear, too often the infant is already damaged. In case of doubt, transfusion is safer than delay.

DR. PHILPOTT (Closing).—I gave our results for cesarean section in hemolytic disease of the newborn, but I will repeat them. We did eight cesarean sections at the thirty-sixth week. We obtained two living babies which were Rh negative. One of the six remaining babies is still alive; the other five all died.

I would like to answer two questions. First, I tried to state what we know, but I did not add that we are working on a new lead. We are studying the blood and effects of liver function. There might be a lead in this direction. Cord blood samples and those taken from the heel are different at the time of birth. We do a photo-electric estimation, and this is

Another thing that has impressed me in seeing these Rh-negative patients, as brought out by the cases of Dr. King is that a very high percentage of these women start their obstetric life with several miscarriages, and yet they have no antibodies at that time. I have noticed this history in a number of patients.

DR. C. L. HUDIBURG, Wilmington, Delaware.—The Rh problem as related to transfusion reactions and hemolytic jaundice or anemia of the newborn is being studied jointly by the laboratory and the Obstetrical Departments of the Delaware Hospital, Wilmington, Delaware. Since January, 1945, the laboratory has performed 1,890 Rh typings, obtaining 11 per cent negative. Routine examinations are performed with 85 per cent serum, and special studies utilize 75 per cent and 30 per cent serums. Antibody titrations use human 4-ORH<sub>1</sub> and 4-ORH<sub>2</sub> indicator cells. Early anti-Rh antibodies are demonstrated by replacing saline with 30 per cent bovine albumin, following the method of Dr. L. K. Diamond.

Two typical cases of hemolytic anemia have been salvaged because of predelivery knowledge of the antibody titer and elective early delivery and transfusion therapy. Another early delivery was lost because of aspiration atelectasis. A fourth case with a low titer was delivered at term and responded well to transfusion therapy. Titration problems presented one case of sensitization which did not increase during pregnancy and delivered as predicted, a normal child Rh<sub>+</sub> (R. K.). Two cases of evident sensitization delivered Rh-negative children. Another case of clinical icterus gravis presented a possible Hr sensitization, with the mother homozygous (pure) positive and the father heterozygous (mixed) positive. Over-sensitization of both doctors and laity to this problem was observed in a case of mild anemia and jaundice in an Rh-negative mother. The child is well and has never shown any antibodies. Rh problems related to transfusions were observed in a case of myelogenous leucemia in an elderly woman who failed to cross-match properly, and evaluation revealed antibodies apparently produced during 11 pregnancies, some of which are known to be positive and negative. Transfusion with negative blood was uneventful.

The serious complication of transfusion reaction was demonstrated in a patient who had received 25 transfusions in twelve years, who had a fatal reaction from Rh<sub>+</sub> cells, but was compatible to Rh<sub>-</sub> cells.

DR. DONALD N. KARIHER, Rochester, N. Y.—In their respective discussions both Dr. Philpott and Dr. King have emphasized the importance of routine Rh tests on all pregnant women. At Rochester we have been attempting to formulate a plan for carrying out this idea for the past two to three years. We have now a scheme which is workable, and, although it has been in operation only eight months, it is proving to be very satisfactory, and I would like to present it briefly to this group.

Since Oct. 1, 1945, the Rochester Health Bureau, in conjunction with the Department of Obstetrics and Gynecology at the Medical School, have been routinely testing for the Rh factor all antenatal bloods sent in for Wassermann tests. The result of the test is reported to the physician on the Wassermann report form. If the patient is Rh positive, nothing further is done. If the patient is Rh negative, a second form is sent the physician along with the Wassermann reports.

This consists essentially of three parts. One portion of the form is for instructing the physician regarding subsequent blood samples. In testing the patient's blood for Rh antibodies, we of course carry out both the agglutinating and blocking techniques.

The husband's Rh status is reported to the physician on a second portion of the form. If the husband is Rh negative, we carry out no further studies, except in individual cases where the history is suggestive of iso-immunization to one of the other blood groups. If the husband is Rh positive, then the physician sends in samples of the patient's blood as requested on the first portion of the form.

Another portion of the form is sent in with the first sample of patient's blood submitted for Rh-antibody determinations. It is the third part of the original form sent to the physician. It makes available to us the expected date of delivery, and the pertinent obstetric history of the patient. On the reverse side of this form is a questionnaire regarding previous transfusions, their dates, and whether the patient had reactions from any of the transfusions.

# THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS IN GYNECOLOGIC PATIENTS; THE PROPHYLAXIS, RECOGNITION, AND TREATMENT\*

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*(From the Massachusetts General Hospital)*

**V**ENOUS thrombosis with its danger of fatal pulmonary embolus is an important problem in the care of gynecologic patients in New England. Prior to 1925, Davis found the incidence of fatal pulmonary emboli to be three in each 1,000 major surgical cases. In the years when exercise, posture, and other conservative measures were used to prevent embolism in the Surgical Wards of the Massachusetts General Hospital, fatal embolism occurred in approximately one out of each 800 major surgical operations. Faxon and Welch, in analyzing cases of deep thrombophlebitis, found that one out of three cases had a pulmonary embolus, and one out of 25 a fatal embolus. Miller and Rogers reported seven deaths out of 206 cases of thrombophlebitis. In patients who had had one infarct, Faxon and Welch found that the second embolus was fatal in 10 per cent of the cases. In patients aged 50 to 70 years with deep thrombophlebitis, the expected mortality is 7 per cent, and if over 70 years of age and suffering from thrombophlebitis, the expected mortality is 20 per cent.

Because of the seriousness of embolism in cases of thrombophlebitis, a means was sought to prevent fatalities from this cause in postoperative patients. Femoral vein ligation had been advocated by several German authors, including Kulenkampf and Fründ, and in this country by Homans and Taylor. The first ligation of the superficial femoral vein at the Massachusetts General Hospital was done in 1937. Since that day in the wards and in the private services of the hospital to December 31, 1945, 1,057 have been done. Early in the study, venography was a part of the method of diagnosis; this method has been discarded, for the venous picture is so very complicated and bizarre that actual and definite knowledge of the presence or absence of a thrombus is hard to determine. Further investigation of the problem was carried out in the autopsy room by Castleman, where it was definitely shown that nearly all fatal emboli come from the veins of the legs. When this fact was established and the pelvic and other veins were ruled out as the usual focus, the treatment and prevention of embolism became possible.

It is the general opinion that, if it could be certain that a clot was present in any given vein, a ligation above that vein should be done at once. The difficult problem is to decide what signs and symptoms are indications of thrombosis. At the present time, it is the consensus of opinion in our hospital that failure to ligate the veins of a patient who has had a nonfatal pulmonary embolus or a patient who has definite signs of either thrombophlebitis or phle-

\*Read at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

done by the same technician. We have found that the hemoglobin estimation is 126 per cent in the blood taken from the heel, and 106 per cent in the blood taken from the cord; this was in a series of 100 cases. We think there is something taking place in the system to cause this terrific hemolysis, and we do know that liver function is tremendously damaged in this disease. We are trying the effects of liver protectives in the hope that they may have something to do with the prevention of hemolysis. We know that vitamin K is absolutely useless in preventing hemolysis in this disease.

With reference to Mr. Rivett's remarks about the leakage of blood, we agree with Hellman and Hertig that there are minute breaks in the intervillous spaces, and therefore little pieces of villi break off and they carry with them fetal red blood cells. When this occurs immunization may take place, and we find that the placenta, liver, and spleen and other organs are affected. We have evidence of marked placentomegaly. When this condition occurs in the placenta, blood can conceivably pass through very easily and it is no longer a good filter.

DR. KING (Closing).—It has been brought out that about only 10 per cent of patients will prove to have an Rh-positive husband and an Rh-negative wife. That reduces the trouble considerably. Although theoretically there should be 150 to 200 with hemolytic disease of the newborn, actually it is about only 1 in 500 deliveries. That has been brought out in Dr. Watson's cases. Actually, there are many who have not been immunized at all.

The method suggested by Dr. Philpott is perfectly logical regarding studies of the placental blood. Only 1/300 of 1 per cent is necessary to immunize a mother.

The question of induction of labor or cesarean section is still undecided. We must also bear in mind the question of transfusion, and if we are in doubt about the Rh type of the recipient, we can always take Rh-negative blood if we have it and it will cause no trouble. So if we have Rh-negative blood available and cannot get the Rh typing of the recipient, we can use that Rh-negative blood.

### General Plan

The general plan of the surgeons, urologists, and gynecologists of our hospital is to try to prevent pulmonary embolism whenever possible by ligating the proper veins in patients who have a suggestion of thrombophlebitis or phlebothrombosis, and to interrupt definitely the femoral veins of those patients who have had a sublethal pulmonary embolus or infarct.

### Signs and Symptoms

In the gynecologic group and in all groups of ward patients, though not so universally on the private services, vein interruption is done upon any suspicion of trouble in the veins of the legs. Table III lists the number of cases who had femoral vein interruption because of pains in their legs.

TABLE III. INDICATIONS FOR FEMORAL VEIN INTERRUPTION

<i>Gynecologic Service—75 Cases</i>					
	1942	1943	1944	1945	TOTAL
Leg signs first symptom	7-87.5%	15-93.4%	14-60.8%	12-42.8%	48
Chest pain first symptom	1-12.5%	1-6.6%	6-26.0%	8-28.6%	16
Prophylactic interruption	0	0	3-13.2%	8-28.6%	11
<i>Massachusetts General Hospital—1057 Cases</i>					
	1937 TO 1942	1943	1944	1945	
Leg signs first symptom	59.0%	56.3%	41.8%	33.7%	
Chest pain first symptom	41.0%	34.5%	32.5%	23.0%	
Prophylactic interruption	0	9.2%	25.7%	43.3%	

The Residents, House Officers, nurses, and the gynecologists and their assistants examine the legs of all postoperative patients during their visits. In the course of the day if any tenderness is found, or the patient complains at all of pain in her legs, a careful examination is carried out. Examination consists of palpation of the groin, the inside of the thigh, the popliteal space, the calf, and the veins of the foot, looking for swelling and tender areas. The most important sign is tenderness in the calf discovered by pressure with the fingers and thumb of the hand. Tenderness of the calf was present in 53 per cent of our group of 75 patients whose veins were interrupted. Next, the foot is brought into dorsal flexion and, if pain is caused, it is very significant (Homans' sign). This maneuver, if done too roughly or forcefully, will cause pain in the calf of most patients, especially in women who have worn high heels, for their Achilles' tendon is short and tight. If Homans' sign is positive, thrombophlebitis or phlebothrombosis is probably present. In the 75 cases, Homans' sign was positive in 28 per cent. The legs are measured by marking an area with ink five inches above and below the patella. If there is an obvious difference in the two legs, and if the swelling is in the tender leg, the diagnosis is definite. A difference of 1 cm. is not sufficient to be of significance, but anything over that, especially if it is apparent both above and below the patella, is very suggestive. The presence of an obviously swollen leg, which has come on suddenly (plus a definitely positive Homans' sign), makes the diagnosis at once. A rise in pulse, temperature, and respiration at the same reading, and it must be on the same reading, and it must be on the same observation, in addition to other physical findings is fairly diagnostic. These changes in the clinical chart, which all of us believe to be of considerable importance as a guide to suggest the presence of a small, unrecognized pulmonary infarct, are called, in our hospital, the "Allen sign," after Dr. Arthur W. Allen, the Chief of the East Surgical Service, who has been so very much interested in this problem. A

bothrombosis *at once* constitutes a serious neglect of the patient. The danger of our present feeling in regard to this phenomenon is that interruption of the femoral vein is probably carried out in patients who do not have anything wrong with their veins, and an unnecessary operation is done. Yet the avoidance of doing a simple procedure to save a patient's life, especially when it is known that the operation is of no serious import, is not to give the patient the best treatment. It is probable and possible that anticoagulents will prove to be satisfactory in the long run, but anyone who has seen a huge blood clot removed from the femoral vein cannot but feel more secure if the vein has been divided.

### Material

The material for this report comes from the public and private wards of the Massachusetts General Hospital. Table I shows the number of cases operated upon each year, the number of veins interrupted, and the deaths from massive pulmonary emboli. These five deaths on the Gynecologic Service stimulated our interest in the problem of thrombophlebitis.

In Table I the types of operations which preceded the vein interruptions are listed, as is the number of patients having presumptive evidence of pulmonary emboli.

TABLE I. GYNECOLOGIC SERVICE WARD AND PRIVATE CASES

NO. OF OPERATIONS		VEIN INTERRUPTIONS	DEATH FROM EMBOLI
1941	355	0	1 (not interrupted)
1942	738	8	0
1943	815	16	1 (not interrupted)
1944	765	23	1 (not interrupted)
1945	830	28	2 (1 interrupted)
Total	3503	75	5

TABLE II. TYPES OF OPERATIONS IN 75 CASES OF FEMORAL VEIN INTERRUPTION

	NO. OF CASES	PRESUMPTIVE EMBOLI
Total hysterectomy	41	7
Vaginal hysterectomy	7	1
LeFort operation	3	2
Plastic operation	7	0
Salpingo-oophorectomy	3	2
Vulvectomy	2	1
Curettage	4	2
Miscellaneous	8	1
	75	16 or 21% (1 fatal)

Allen, Linton, and Donaldson have shown in their studies the value of vein interruption in the surgical group. Colby has shown, and is convinced in its value in the cases of the urologic group. In the elderly male patients of the Urologic Service, and it is in this older group that fatal pulmonary embolism usually occurs, there can be no doubt of the value of vein ligation. Colby reports the incidence of fatal pulmonary emboli occurring in patients operated upon for prostatic obstruction. In 1939 to 1940, when there were no vein interruptions, there were eight fatal pulmonary emboli in 302 operations; while in 1943 to 1944, there were nine femoral vein interruptions and there were only four fatal emboli in 428 operations—a reduction in percentage from 2.63 to 0.93, ascribable to vein interruption and early ambulation.



The surgical treatment of thrombophlebitis and phlebothrombosis consists of the interruption of the vein above the clot. Both legs must be operated upon, for if thrombosis has occurred on one side it may be present on the other and patients have died when the apparently affected vein alone has been tied, the other leg being the source of the embolus. It is always necessary to operate on both sides. Note in Table IV the shift from unilateral to bilateral femoral vein interruption on the Surgical and Gynecologic Service.

TABLE IV. FEMORAL VEIN INTERRUPTION

NO. OF PATIENTS		VEINS	UNILATERAL	BILATERAL
<i>Massachusetts General Hospital, 1937-1945</i>				
1937-1942	202	280	61.0%	39.0%
1943	165	299	19.0%	81.0%
1944	280	554	2.1%	97.9%
1945	410	816	0.98%	99.0%
	1057	1949		
<i>Gynecologic Service, 1942-1945</i>				
1942	8	13	37.5%	62.5%
1943	16	31	6.3%	93.7%
1944	23	46	0	100%
1945	28	56	0	100%
	75	146		

The choice of the anesthetic depends upon the apprehensiveness and condition of the patient. If she is calm, local anesthesia is satisfactory; if apprehensive, pentothal or gas, oxygen, ether is indicated.

The femoral arterial pulsation is palpated in the groin and a 4-inch incision is made downward along the course of the artery. The subcutaneous tissue, superficial fascia and fascia lata are divided. The femoral pulsation is felt for and deep to the sartorius muscle and lying on the adductor longus muscle, the femoral artery and vein are found. The artery is anterior and slightly lateral to the vein. The long saphenous nerve lies on the outer side of the artery and should be avoided. The sheath overlying the vessels is approached from the medial side and the sheath surrounding the vein opened. Inside the sheath the dissection is carried upward and the profunda femoris perforates the muscles posteriorly about an inch and a half below Poupart's ligament. There is a bulbous swelling of the superficial femoral vein at this junction. The junction should always be well visualized and the superficial femoris isolated over a four centimeter length. When the vein is located and isolated, ligatures are placed under the vein and not tied. These are held on tension and the vein opened, tension is released to see if there is a free flow of blood. Occasionally when the vein is opened a clot may extrude from above and if this is followed by a free flow of blood it is not necessary to suck out the upper or proximal part of the vein. A large clot may slip spontaneously from the distal femoral vein out the opening. Recently a clot with all its branches at least 18 cm. long came out this way. This patient's life was probably saved. If there is no flow of blood from above after the opening of the vein, and there should be, it is essential to use suction to remove the suspected clot. The suction apparatus with a bent glass drinking tube on its end is placed up into the common femoral vein with the suction on. After the vein is sucked out and a free flow of blood occurs, the common femoral and iliac veins are considered cleared. Occasionally the profunda vein is involved by a thrombus, as well as the superficial femoral. It is important to note this because then it is necessary to tie off the common femoral rather than the superficial. To prove that the profunda is not involved, it is necessary to shut off the flow of blood from the superficial and common

patient with marked phlegmasia alba dolens with edema of the leg, thigh, and lower abdomen is a problem that is not pertinent to this paper. In such cases the thrombus is generally in the common femoral, possibly in the iliaes, and probably involves the lymphatics of the retroperitoneal region about the large pelvic veins. This problem should not be encountered in postoperative patients, for signs and symptoms of thrombophlebitis should have manifested themselves sufficiently to suggest vein ligation before such an end result is reached. If a patient with an old phlebitis is to be operated upon, it is the duty of the surgeon on the Gynecological Service to tie off the superficial or common femoral vein before operation or at the conclusion of operation as a prophylactic measure. This is one of the problems of prophylactic vein ligation and will be considered later.

### Prophylaxis

Various methods have been tried to prevent the formation of phlebitis or thrombosis in the legs of postoperative patients. The patients, while helpless in bed, are rolled from side to side, and the legs are flexed and extended as soon as passive motion is possible. Active exercises are carried out by every patient as soon as they are conscious. Later, they are watched while doing their bicycle exercise two to three times per day. As soon as the patient reaches her bed after operation the foot of the bed is elevated upon eight inch blocks so as to aid in draining the leg veins. Pillows are not allowed under the knees. The morning after operation the blocks are taken out from the foot of the bed and are placed under the upper part to raise the head of the bed. A foot board is placed at the bottom of the bed, and the patient is urged to keep herself up in bed by pressure with her feet against the foot board. This is satisfactory during the daytime but is omitted at night, for it interferes with sleep. Bicycle exercises are kept up until the patient is out of bed. Early mobilization (first, second, or third day) has been the rule until very recently. Lately, because many gynecologic patients are fatigued, anemic, and worn out, and need rest as well as surgery, early mobilization has been changed to allowing patients out of bed when they ask to get out, and always before the tenth postoperative day. Early mobilization may have caused some postoperative complications, especially when patients sit in low, comfortable chairs that are present in most hospital rooms. It is much safer to allow them to stand up and move about without sitting or, if they must sit, to sit upon a high chair or stool so that acute flexion at the hips does not occur.

Anticoagulants are not used as a routine on the Gynecological Service. There is no doubt of their value, and a very carefully controlled group of patients are being followed on the wards by Dr. Allen. This control series will be compared with the present series later, and should give us some inkling as to the prophylactic value of anticoagulants. If an embolus follows ligations of veins, and it can and does occur, but not fatally, dicoumarol is given for ten days, making sure that the prothrombin time is definitely raised. If the prothrombin time is not changed, the value of dicoumarol is certainly open to question.

### Treatment

In the past, the treatment of phlebitis or phlebothrombosis has been immobilization of the affected part and the use of hot or cold packs. The leg rested upon a pillow and the patient was not allowed out of bed until her temperature had been normal for at least a week.\*

\*During this treatment the patient sometimes had a pulmonary embolus or developed a typical phlegmasia alba dolens with its prolonged convalescence and its occasional permanent disability. Interruption of the superficial femoral veins markedly shortens the convalescence. In the General Surgical Group (Allen, Linton, and Donaldson) the average number of days from vein interruption to a normal chart was 5.3, and the average number of days from vein interruption to discharge from the hospital was only 8.9 days.

TABLE V. AGES BY DECADES

<i>Massachusetts General Hospital Cases—367</i>			
<i>1937-1943</i>			
0-10	1	0.3%	
10-20	6	1.6%	17.7%
20-30	14	3.8%	
30-40	44	12.0%	
40-50	68	18.5%	
50-60	93	25.3%	
60-70	84	22.9%	82.3%
70-80	48	13.1%	
80-90	7	1.9%	
90-100	2	0.6%	
	<u>367</u>		
<i>Gynecologic Cases—75</i>			
<i>1942-1945</i>			
10-20	0	0	
20-30	5	6.7%	28.0%
30-40	16	21.3%	
40-50	22	29.3%	
50-60	13	17.3%	
60-70	11	14.7%	72.0%
70-80	7	9.3%	
80-90	1	1.3%	
	<u>75</u>		

the profunda. There was an older clot in the common femoral vein that did not connect with the clot in the superficial femoral stump. It could be argued that either the common femoral vein was not properly explored or that the clot in the common femoral was caused by the clot in the stump of the superficial femoral vein. This calamity has made us realize that it is essential to tie the vein off close to the profunda and that prophylaxis at the time of operation is probably better than 2 to 3 days later.

### Results

There has been no immediate mortality from the operation for ligation of the femoral veins and, except for an occasional lymphorrhea from the wound, no serious complications have occurred. In other hands the femoral artery has been mistaken for the femoral vein and ligated. This is mentioned only because *it has been done*. There is a little postoperative morbidity. Swelling of the legs after ligation of the superficial femoral vein may occur but it does not persist after six to twelve months. If it persists after twelve months, it is reasonable to feel that a true phlebitis had been present at the time of operation, and it is well known that swelling does occur after phlebitis. Superficial vein ligation by itself should be without any sequela. Common femoral vein ligation, however, is followed by swelling of the legs in a larger percentage of cases. If the saphenous vein and the common femoral vein are both ligated, it is quite likely that swelling of the leg will follow. In cases where the saphenous has been previously ligated, it is well before tying off the common femoral vein, to see how much venous pressure there is in the distal femoral vein before ties are placed about the common femoral. The superficial femoral can be tied safely along with the saphenous but when all three are to be ligated, due consideration should be given to the filling of the distal vein before ligation. Tension in that vein should indicate that the surgeon should not be too radical.

To our knowledge emboli have never occurred at the time of ligation or during the use of suction in the removal of clots from above. Emboli have followed interruption of the veins but few have been fatal. Emboli following

femoral veins. If there is a free flow of blood from the profunda through the venous incision then it is considered open. If the profunda and the common femoral are open or cleared out, interruption of the superficial femoral may be carried out. This is done by means of silk ligatures just below the profunda, for if not a clot may form in the stump of the superficial femoral which may propagate and lead to an embolus. In a personal series of cases this phenomenon has occurred three times. Interruption is now always done at the profunda branch. It is safest to place one stitch ligature through the vein for occasionally a tie may be forced off and this may prove to be very embarrassing. If the superficial femoral and the profunda are involved, it is essential that the common femoral vein be ligated. This ligation is carried out below the area where the saphenous vein empties into the femoral, for it is not wise to tie off all the veins. A small dressing is placed over the wound, no leg bandages are applied, and the patient sent back to bed. Bed exercises are continued and the patient is allowed out of bed the same day, or at least by the next day.

Occasionally it may be necessary to go still higher than the common femoral vein and ligate the iliac veins or the vena cava. Ligation of the common iliac veins of the right side of the pelvis is much easier than the left side, due to the position of the left common iliac behind the sigmoid mesentery and behind the left common iliac artery. Ligation of the external iliac veins is very simple but it is not the operation of choice for abdominal varicosities may develop from the branches of the saphenous at its femoral junction. Prophylactic ligation of the external iliac veins at the time of total hysterectomy is very simple and although it has been done a number of times and no untoward developments have yet occurred, nevertheless it will be avoided until more information about abdominal varicosities is obtained. Vena cava ligations done either through the posterior peritoneum or retroperitoneally are not difficult and in patients with pelvic phlebitis this operation should be seriously considered. It has been done a great many times and the results are not too serious. In a few cases the legs have shown a tendency to swell and become ulcerated, but saving the life of the patient makes this complication very minor.

### Prophylactic Interruption

Although most of the surgeons of our hospital agree about ligation of veins for early thrombophlebitis or phlebothrombosis we are not all in agreement about the prophylactic interruption of veins. Inasmuch as most fatal emboli occur in patients 60 years of age or older, it has been considered wise at the time of operation to interrupt the superficial femoral vein to prevent the occurrence of emboli. This procedure can be done easily after the operation has been concluded. Table V compares the ages of the general surgical cases as presented by Allen and his co-workers and our series of 75 cases, and shows the relative high incidence of thrombo embolic disease in the older age groups.

In our experience, ligation of veins adds but very little to the shock of the operation and delays it but a short time. In patients who have had phlebitis or a previous embolus following a previous operation, this maneuver would seem advisable. The ligation is often done in our hospital either 2 to 3 days after the original operation or at the time of the operation. It should be done at the time of operation for in the 2 to 3 days following the operation a thrombosis may have occurred. In one heartbreaking experience ligation of the veins was done three days after operation, the ties were placed  $1\frac{1}{2}$  inches below the profunda and on the fourteenth day the patient died of a fatal pelvic embolus. Because of the ligation the diagnosis of pulmonary embolus was not made, and she was considered to have a coronary thrombosis. At autopsy, a small clot was found in the stump of the left superficial femoral vein between the tie and

## PHLEBOTHROMBOSIS AND THROMBOPHLEBITIS IN GYNECOLOGY AND OBSTETRICS\*

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IT IS extremely important that physicians realize the full import of the complications and sequelae occasioned by intravenous clotting. Every physician is naturally upset when one of his patients dies, but he is usually less disturbed if the death is due to pulmonary embolism than to peritonitis or some other cause. In the former case, he believes that the death was unavoidable; in the latter case he thinks that death might have been prevented. Yet, the advances made in the past decade in our knowledge of intravenous clotting make us wonder whether or not death from this complication should not be classified as preventable. Similarly, should not the same be true of the sequelae?

Intravenous clotting is of two types, phlebothrombosis and thrombophlebitis. Phlebothrombosis has been defined as a "partial or complete venous occlusion by an intravascular clot which is unassociated with inflammation, the clot being loosely attached to the vein wall."<sup>42</sup> Because of its loose attachment, this type of thrombus is the one most likely to break away and result in pulmonary infarction and embolism. Thrombophlebitis is "a partial or complete venous occlusion by an intravascular clot which is associated with, and dependent upon inflammation of the vein wall."<sup>42</sup> In thrombophlebitis the clot is strongly adherent, and, unless suppuration is present, rarely results in pulmonary infarction or embolism.

### Etiologic Factors

The etiologic factors involved in intravenous clotting are cardiovascular lesions,<sup>1-4</sup> varicosities,<sup>5-7</sup> vasoconstrictors,<sup>8</sup> obesity,<sup>5, 6, 9, 35</sup> focal infection,<sup>5, 8</sup> cancer,<sup>10</sup> dehydration and demineralization,<sup>11</sup> anemia,<sup>12-15</sup> trauma,<sup>8, 16-21</sup> sepsis, circulatory collapse,<sup>22</sup> chilling,<sup>23</sup> posture,<sup>24-28</sup> immobilization,<sup>16, 17</sup> abdominal distention,<sup>34</sup> interference with full respiration,<sup>29-33</sup> and mechanical retardation of the venous flow and advancing age.<sup>36</sup>

Some authors<sup>37, 38</sup> consider thrombophlebitis a later stage of phlebothrombosis, but all recognize that intravascular clotting can be of two types, phlebothrombosis and/or thrombophlebitis. In thrombophlebitis the clot can undergo liquefaction as a result of infection and produce purulent septic phlebitis (suppurative phlebitis). This is especially true in cases of pelvic thrombophlebitis occurring in postpartal or postabortal sepsis, where the thrombotic process begins in the vessels of the placental site, the veins of the uterine wall or

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vein interruption is usually due to faulty technique and should not occur if the operation is done correctly. If emboli do occur they are not fatal and the use of dicoumarol has prevented further emboli.

After ligation of the veins of the legs, even if there are signs of a definite phlebitis, early mobilization may be carried out. Often the legs are tender after ligation for there may be a clot below the point of ligation and distention occurs due to this clot and is responsible for the tenderness. Some believe that post ligation tenderness is indicative of the fact that there was a phlebitis present before operation. It is more likely that a clot has been formed due to the ligation and distention of the vein caused tenderness.

Clots were found at the time of ligation in 19 per cent of the patients operated upon on the Gynecologic Service. It is most satisfying to find clots in the veins at the time of ligation because the operator feels he has accomplished something. It is much safer, however, to operate when thrombosis is thought to be present and to believe that the operation was done before propagation of the clot occurred.

### Conclusions

1. All the surgeons of the Massachusetts General Hospital are convinced that interruption of the femoral veins is essential after a sublethal embolus or infarct.

2. Nearly all are agreed that interruption of the femoral veins is essential after the diagnosis of thrombophlebitis or phlebothrombosis has been definitely made.

3. The danger to the patient from interruption of veins properly done is minimal and it is apparent that the operation is a lifesaving one.

4. Morbidity and mortality are extremely small in the surgical attack upon thrombosis in the veins of the legs.

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(For Discussion, see p. 959.)

Present-day concepts in the management of phlebothrombosis are represented by two schools of thought. Allen,<sup>38</sup> Ochsner,<sup>40, 41, 42</sup> Homans,<sup>39</sup> Evans,<sup>48</sup> and their co-workers favor venous ligation above the thrombotic process, even if it be necessary to ligate the vena cava. Bauer,<sup>37</sup> Crafoord and Jorpes,<sup>40</sup> Evans,<sup>48</sup> and others advocate both the prophylactic and therapeutic use of dicoumarol or heparin. We have had no experience with the use of heparin or dicoumarol, but have used the surgical treatment for this complication.

The incidence of pulmonary embolism following gynecologic operations reported in the past three years at first glance seems small. However, when it is realized that this complication accounts for from 12.3 per cent to 25 per cent of all deaths following gynecologic operations,<sup>50-52</sup> its importance becomes apparent. By means of improved technique, better anesthesia, good pre-operative preparation of the patient, sulfonamides and antibiotics, plasma, and blood transfusions, the mortality rate following surgical procedures on the female pelvis has decreased materially. Deaths from hemorrhage and sepsis have declined, but pulmonary embolism remains a major problem. As stated previously, the greater number of pulmonary emboli and infarcts occur from thrombi arising in the area drained by the vena cava. The incidence of thrombophlebitis and phlebothrombosis following pelvic operation varies in reported series from 0.65 per cent to 3.9 per cent<sup>50, 53, 56</sup> in the former and 0.16 per cent to 1.3 per cent in the latter.<sup>55, 56</sup> It is interesting to note that in the series studied only two reports differentiate between phlebothrombosis and thrombophlebitis, namely, those from Boston and New Orleans, from which most of the literature pertaining to these complications has emanated. It is extremely important to differentiate these two types of intravascular clotting, since different methods of therapy are indicated in each.

At Charity Hospital in New Orleans during the period July 1, 1939, to Jan. 1, 1946, there were 32,198 admissions to the gynecologic service, and a total of 536 deaths from all causes, exclusive of abortion. A study of the records of all deaths and autopsy records, when autopsy was obtained, showed that intravenous clotting was present in the pelvic veins in 50 cases. No mention is made of routine examination of the veins of the lower extremities. If such an examination had been made, and if autopsy had been performed on all patients who died, undoubtedly the incidence of intravascular clotting found in the channels of the inferior vena cava would have been higher. This gives a minimal, irreducible, and uncorrected incidence of 9.3 per cent in this series of 50 cases of proved intravascular clotting in 536 gynecologic deaths. In these 50 autopsies, pulmonary embolism was found to be present in 12 cases of phlebothrombosis and four cases of suppurative thrombophlebitis of the pelvic veins. The latter will be discussed later in this presentation. Of the 12 cases of pulmonary emboli, six occurred following operations on the female pelvis, particularly hysterectomy for uterine fibroids, although one followed repair of a urethral diverticulum. In this latter case, in addition, the patient had a "trophic ulcer of the left leg" which no doubt played a part in the production of the intravenous clot.

More important than the deaths recorded from pulmonary emboli following operation is the fact that five of these fatal emboli occurred in patients who were not operated on, but who were being prepared for operation for a pelvic tumor associated with edema of the lower extremity or extremities, the



pampiniform plexus, or in the vagina, and extends into the uterine, ovarian, hypogastric, iliac, or renal veins, and not infrequently into the vena cava.

In phlebothrombosis or thrombophlebitis, unassociated with puerperal sepsis, the intravascular clot originates, in a considerable number of cases, in the lower part of the leg.<sup>37, 39, 40-43</sup> Ingraham,<sup>44</sup> in a study of 246 unselected autopsies, observed thrombosis of veins of the pelvis or legs in 28 instances (11.4 per cent) whereas Pretten<sup>45</sup> found that in 133 out of 144 fatal emboli the thrombus originated in the region drained by the vena cava. McCartney<sup>46</sup> noted the frequency of thrombosis of the deep veins of the leg among middle-aged and old persons forced to bed for varying periods of time, the incidence of thrombosis being 52.7 per cent, with bilateral involvement 110 times and unilateral involvement 75 times. Although less frequent in younger individuals, the same can occur in any patient of any age who is forced to bed for a long period of time or whose lower extremity or extremities are immobilized for one reason or another.

### Phlebothrombosis

The fact that the signs and symptoms of bland intravascular clotting are minimal makes the diagnosis of phlebothrombosis exceedingly difficult unless its possibility is constantly kept in mind. Unlike thrombophlebitis, there is usually little or no swelling, pain, or fever, and sometimes pulmonary infarction or embolism is the initial symptom.<sup>38, 47</sup> Any persistent or undue elevation of the temperature, pulse, or respiration should arouse suspicion, and repeated examination for clinical signs of phlebothrombosis should be made.<sup>38</sup> Homans' dorsiflexion sign, a valuable diagnostic adjunct, was found in 139 of 237 cases in Allen's series. This same author found some degree of swelling and tenderness in the greater proportion of his cases. Examination of the legs should be a part of the routine of the postoperative or postpartal care of patients confined to bed. A complaint of pain in the chest or ache or pain in the lower extremities, no matter how slight, should not be casually dismissed. In some cases, marked edema of the leg is found in phlebothrombosis, especially if the common femoral vein is involved. This is more evident in cases of tumors of the pelvis in which the edema and swelling is too often ascribed to pressure by the tumor and the true etiology is undiagnosed. Any case of unilateral edema, and particularly those associated with pregnancy or pelvic tumors, should be considered to be due to phlebothrombosis of the femoral or pelvic veins until proved otherwise. Grave and fatal embolism will result if particular care is not taken to rule out this condition.

The treatment of phlebothrombosis varies in different clinics. The time honored and, in our opinion, "horse and buggy" therapy—swathing of the leg in cotton batting and elevation of the affected part—is still all too frequently employed. Certainly, it does not prevent pulmonary infarction or pulmonary embolism and, although the patient may survive the prolonged convalescence, the possibility of postphlebitic edema and ulceration leaves much to be desired when this method of therapy is used.



TABLE I. PHLEBOTROMBOSIS AND THROMBOPHLEBITIS AND PULMONARY EMBOLISM IN GYNECOLOGY

AUTHOR	YEAR	NO. OF CASES	TYPE	THROMBO-PHLEBITIS	PHLEBO-THROMBOSIS	DEATHS	NONFATAL EMBOLI	FATAL PULMONARY EMBOLI
Gaston <sup>53</sup>	1945	130	Total abdominal hysterectomy	5 (3.90%)			1 (0.77%)	0
Mengert and Stoltz <sup>50</sup>	1945	1,925	Total abdominal hysterectomy	27 (1.40%)		38		6 (15.9%)
Tritsch and Sagarra <sup>51</sup>	1944		Hysterectomy			12		3 (25.0%)
Jones	1943	800	Abdominal hysterectomy	13 (1.62%)			6 (7.50%)	5
Solomon <sup>52</sup>	1942	790	Abdominal hysterectomy			17		2 (12.3%)
Evans and Kassel <sup>55</sup>	1945	381	Pelvic operations	2 (0.55%)	5 (1.30%)		5 (1.30%)	0
Counselor and McKinnon <sup>6</sup>	1942	2,684	Abdominal hysterectomy	99 (3.70%)				
Tyrone et al. <sup>56</sup>	1946	609	Hysterectomy	4 (0.65%)	1 (0.16%)		1 (0.16%)	0

TABLE II. PHLEBOTROMBOSIS AND THROMBOPHLEBITIS AND PULMONARY EMBOLISM IN OBSTETRICS

AUTHOR	YEAR	CASES	TYPE	THROMBO-PHLEBITIS	PHLEBO-THROMBOSIS	DEATHS	NONFATAL EMBOLI	FATAL EMBOLI
Davis et al. <sup>57</sup>	1946	47,945	All			81		6 (7.40%)
Gough <sup>58</sup>	1946	6,000	All			10		2 (20.00%)
Minnesota Maternity Mortality Study <sup>59</sup>	1944		All	9		112		9 (8.00%)
Rosensohn et al. <sup>60</sup>	1944	494	Cesarean section			17		1 (5.90%)
Hobbs <sup>61</sup>	1943	18,539	All			42		2 (4.76%)
Spain et al.	1944	4,243	All	6 (0.14%)				0
Ochsner Clinic	1946	1,007	All	1 (0.10%)	0		0	0
Falkner	1944	5,420	All	4 (0.07%)			1	0

latter being ignored and probably assumed to be due to pressure by the growth. In the light of our present-day knowledge of phlebothrombosis, these deaths may be considered to have been preventable. In contrast to the five cases of fatal emboli just mentioned, there were three patients, admitted to the Tulane Gynecologic Service at Charity Hospital with the same syndrome, in whom phlebograms confirmed the presence of phlebothrombosis and, at operation by the senior author, the left common iliac vein was found thrombosed to the formation of the vena cava; recovery without ill effects followed ligation of the vena cava and hysterectomy. There is no way of proving that these patients would have died had not ligation above the thrombus been practiced, but in the light of the five patients with the same syndrome who died while undergoing preoperative care, this conclusion seems justifiable. To reiterate, we believe that any patient with unilateral edema of the extremity either with or without pelvic tumors should be considered as having an intravascular clot of the common femoral and/or iliac vessels until proved otherwise, and vein interruption should be the first step in the care of the pelvic lesion.

In recent reports concerning maternal mortality, the incidence of fatal pulmonary emboli varies from 4.7 per cent to 20 per cent<sup>57-61</sup> of all obstetric deaths. At Charity Hospital in New Orleans there were three deaths due to pulmonary embolism in 194 deaths reviewed by the author, an incidence of 1.5 per cent. In our series, nearly all cases of pulmonary infarction or embolism followed suppurative pelvic thrombophlebitis, and this will be discussed later in this presentation.

### Thrombophlebitis (Phlegmasia Alba Dolens)

As contrasted with phlebothrombosis, the diagnosis of thrombophlebitis of the veins of the extremities is not difficult. Usually fever is present; there is a great deal of pain, a variable degree of swelling, ranging from mild pitting edema to massive edema, tenderness along the course of the involved vein, and in cases of deep vein involvement, particularly the femoro-iliac veins, pallor and cyanosis in the involved extremity. The swelling is not totally due to increased venous pressure resulting from venous blockage by the thrombus, but is partly due to accumulated perivascular fluid.<sup>40</sup>

Ochsner and DeBakey<sup>40</sup> have shown that as a result of venous blockage there is a reflex vasospasm throughout the vascular tree of the involved extremity and, as a result, arteriolar pulsations are diminished producing capillary stasis and consequent anoxia of the capillary endothelium; consequently, capillary permeability is increased with exudation of fluid into the perivascular spaces, producing a vicious circle. Not infrequently, following subsidence of the acute inflammatory process, the patient continues to have considerable edema or other undesirable sequelae for the rest of her life. Here, the persistence of symptoms is probably due to perivascular fibrosis, the production of which is favored by lymph stasis. Following blocking of the sympathetic nerve supply to the involved extremity, the vasospasm can be overcome; this results in a decrease in venous pressure, diminished filtration pressure, and a tendency to prevent the increased transudation into the perivascular spaces. In addition, normal arteriolar pulsations re-establish the oxygenation of the vascular endothelium and return the permeability of this membrane to normal. Furthermore, the return of normal pulsation increases the flow of lymph and its removal of perivascular fluid.

recent years have consulted the gynecologists in case of pulmonary infarction occurring in the female in order to rule out the pelvis as a focus. Consequently, the number of cases of this condition terminating fatally on the medical wards has been reduced in the past few years.

To appreciate fully the problem of postabortal and postpartal sepsis and septic deaths in gynecologic disorders encountered in an institution like Charity Hospital in New Orleans, which serves as a "dumping ground" for all types of cases throughout Louisiana, one needs only to review the following figures. During the period July 1, 1937, to Jan. 1, 1946, of 32,198 patients exclusive of abortion admitted to the gynecologic wards of Charity Hospital, 536 died.

As stated previously, of the cases autopsied, 50, or 9.3 per cent, showed intravascular clotting in pelvic veins. In 12 instances bland clotting or phlebotrombosis was found, but, in the remaining 38 cases, suppurative pelvic thrombophlebitis was present and followed all types of gynecologic operations. A large number (11 cases) was associated with cul-de-sac or tubo-ovarian abscesses. This is not surprising, for here we have patients confined to bed for a long time with a suppurative process in intimate relation with the large pelvic veins—two of the most common etiologic factors producing thrombophlebitis. Certainly, earlier surgical drainage of pelvic abscesses, as well as particular attention to having these patients move the extremities many times a day while in bed, is indicated if the complicating factor of suppurative pelvic thrombophlebitis is to be prevented. Fatal pulmonary embolism occurred four times, due to detachment of clot, by the suppurative phlebotic process. In one case of suppurative pelvic thrombophlebitis with pulmonary infarction, following vaginal hysterectomy, vena cava ligation was performed with immediate recovery and no untoward effects. During the same period there were 44,027 deliveries at the same institution and 6,314 cases of abortion. In the former, there were 194 deaths, and in the latter, 70, a total of 264 maternal deaths in 50,341 cases, or 0.53 per cent.

Autopsy was not performed in all these cases; however, of the cases autopsied, 31 showed intravascular clotting of the pelvic veins, an uncorrected incidence of 11.7 per cent for all deaths, or 35 per cent of deaths due to puerperal sepsis. Undoubtedly, a greater percentage of autopsies (coroner's cases), especially of fatal abortion, would have materially raised this figure. In nine cases pulmonary infarction was found, and in three additional cases pulmonary embolism was observed. Again, the fact that an active suppurative process is present in the clot allows for liquefaction and infarction or embolism. Of course, the statistics just cited do not include patients having puerperal sepsis whose hospital course and history of infarction led to a diagnosis of pelvic (suppurative) thrombophlebitis and who died but on whom autopsy was not performed, nor do they include the patients operated on in whom the presence of intravascular clotting in the pelvic veins was proved or those who recovered under medical regimens.

Although the mortality rate in puerperal sepsis has been reduced by the advent of chemotherapy and antibiotics,<sup>57, 63</sup> it is still a leading cause of death in postabortal and postpartal sepsis.<sup>71-79</sup> Undoubtedly, the early and proper administration of these therapeutic agents is responsible for a considerable decrease in fatal cases, the fact remains that all cases are not cured by their administration.

Another factor to consider in statistics concerning deaths due to sepsis in obstetrics is whether one follows the patient throughout the course of pregnancy or the patient suddenly has been thrust upon him with a well-developed sepsis already present. The same can be said of the time interval between the performance of a criminal abortion and admission to a hospital. In two-thirds of the deaths occurring from postabortal sepsis at Charity Hospital, the

The incidence of thrombophlebitis of the extremities following gynecologic operations at Charity Hospital is about 0.12 per cent. In our private practice, the incidence is 0.16 per cent. This is lower than that of collected series<sup>50, 53-56</sup> from other sections, and is probably due to several factors, of which climatic conditions and prophylactic therapy play important roles. The incidence of this complication following delivery is fairly constant in all reported series. At Charity Hospital in New Orleans, the incidence is 0.06 per cent, and in our private practice, 0.1 per cent.

Infarction and embolism in thrombophlebitis of the extremities are rare but these complications, although not dangerous to life, can prolong convalescence and may produce disfigurement and disability; for these reasons alone the importance of proper and early application of therapeutic measures is evident. As in phlebotrombosis, the time-honored treatment has consisted of elevation of the leg, application of cotton batting and heat tent, and, in some instances, application of leeches along the course of the involved vein, roentgen rays and continuous caudal anesthesia, vein ligation, heparin, and dicoumarol. However, today, we believe that the treatment *par excellence* of this complication is lumbar paravertebral sympathetic block with procaine hydrochloride as advocated by Ochsner and DeBakey. The relief from pain is dramatic and the early and permanent subsidence of edema and fever together with the fact that convalescence is noticeably shortened leave little to be desired in this form of therapy. The technique is simple and may be applied anywhere; no special equipment is needed. This method of therapy has been used at Tulane University since 1938 with consistently excellent results.

### Suppurative Thrombophlebitis of the Pelvic Veins (Septic Phlebitis)

Because of its frequency as a cause of prolonged convalescence and serious complications including death, suppurative thrombophlebitis of the pelvic veins is of much interest and importance to the gynecologist and obstetrician. This condition is most frequently found in cases of puerperal sepsis (either postabortal or postpartal), although it may follow the application of radium to the female genitals, operations on the female genital tract, and suppurative processes in the adnexa.<sup>64</sup> In large general hospitals, such as Charity Hospital in New Orleans, with large clinics, large inpatient services, and no restrictions, except financial, as to who is eligible for admission, all types of cases of post-operative postpartal or puerperal sepsis are frequently encountered.

*Incidence.*—In an attempt to find the approximate incidence of suppurative pelvic thrombophlebitis occurring in females at Charity Hospital in New Orleans, we reviewed all deaths occurring in females during the period from July 1, 1937, to Jan. 1, 1946. A number of the patients during the early years of this study died on medical wards where the true etiology of the condition remained unrecognized. Some were admitted with pulmonary infarction or a diagnosis of pneumonia. Since publication of an earlier preliminary survey<sup>64, 65</sup> of this condition and the results following operation when medical therapy failed, the internists have become aware of the important relations between pulmonary infarction and the female pelvis, and consequently in



abortion preceded admission to the hospital by ten days or more, a few patients being moribund on admission. At Charity Hospital, as elsewhere, there has been a material reduction in the deaths due to puerperal sepsis since the advent of chemotherapy and penicillin, but fatalities still result.

The routine management of abortion on the Tulane Service at Charity Hospital has been changed but little since 1928. The conservative tenets<sup>80</sup> set forth by our preceptors, the late Drs. C. Jeff Miller and Hilliard E. Miller, are still closely followed, the only addition being penicillin and an earlier and more complete ligation of the venous return from the uterus in cases failing to respond to conservative therapy.

The question of the value of venous ligation in the treatment of puerperal sepsis<sup>84-86</sup> is an old one, there being great diversity of opinion as to when to ligate, what veins to ligate, whether or not the patients would not have survived without operation, and whether the percentage salvage following operation justifies such a procedure. Our primary interest as physicians is saving lives and we are convinced after observing a large number of cases over a period of eighteen years that the operative management of cases of suppurative pelvic thrombophlebitis failing to respond to conservative therapy will save lives that otherwise would be lost.

Miller<sup>66, 67</sup> and Miller<sup>68</sup> reported some of their cases of venous ligation; the results were sometimes brilliant, sometimes depressing. In retrospect, we believe that some of the failures were due to the fact that the operation was performed too late in the course of the disease, and the normal venous return from the uterus was not interrupted. One of us (C. G. C.) also had failures before the decision was made to ligate the vena cava and ovarian veins routinely in cases in which the conservative regimen was of no further avail and operation was indicated.

A definite diagnosis of suppurative pelvic thrombophlebitis is fairly difficult to make. Other causes of fever and/or chills must first be eliminated. A history of delivery, abortion, operation, or application of radium is usually obtained, and the patient's pulse, respiration, and temperature closely followed. If spiking fever and chills are present, less difficulty is encountered, but all patients do not show these characteristic signs or symptoms. In occasional cases, a plateau-like temperature curve is found and chills may be absent. A fairly constant finding is an elevated pulse and a patient who does not look as sick as the findings would indicate. On vaginal examination, little or no exudate is found in the parametrial areas, and occasionally one can feel the thrombosed veins, but this is not a constant finding.

Thrombosed veins should be looked for not only in the parametrial area, but along the whole vaginal wall. In one case (No. 13) we were able to palpate a large thrombosed vein extending from an infected episiotomy wound up and into the parametrial areas. In an earlier report<sup>64</sup> we showed that 85 per cent of these cases had infarction into the lung, and that all lung infarcts do not produce the typical pleural pain and bloody sputum, but can be silent. As many infarcts can be detected only by means of roentgenograms, chest plates are routinely made in all patients showing sepsis, and the roentgenogram of the chest is repeated if the patient fails to respond to conservative therapy. The frequency with which small pulmonary infarcts are erroneously diagnosed by roentgenograms has been previously reported by us,<sup>64</sup> and more recently by Krause,<sup>69</sup> who states "The roentgen diagnosis of pulmonary infarct is probably subject to a greater percentage of error than that of any other lesion of the lung."

Blood cultures are of value if the result is positive, especially in determining whether or not the organism is penicillin-resistant or sulfa-fast. However, if negative, it in no way rules out the presence of suppurative pelvic thrombophlebitis.

tion and resulting lung abscess. During that period of time she was perfectly well, had no edema of the extremities, and engaged in all types of social, athletic, and household activities. Another patient (Case 8) died of third degree burns incurred celebrating V-J day three years after ligation. Up until death she was perfectly well, in excellent health, and had no edema of the extremities or complaint of any kind. The third death (Case 1) occurred from hemorrhagic encephalitis following arsenical therapy for syphilis two years after ligation. The remaining patients show no edema of the extremities. There are no dilated abdominal, thoracic, or peripheral veins, and activities of all types are unrestricted. Three have become pregnant since and aborted, whereas one has delivered two full-term children. In no patient was there any antepartal, intrapartal, or postpartal complication of any sort. Vaginal examination on all revealed no evidence of any lesions or varicosities of the vulva or vagina. Hemorrhoids were not present.

Dr. George Burch and his co-workers<sup>81, 82</sup> of the Department of Medicine at Tulane University have studied these patient's circulatory status in the lower extremities at regular intervals and state: "Although the venous pressures of the lower extremities remained elevated and the volume of pulsations of the toes was reduced, there were no objective ill effects noted in the lower extremity as long as four years following operation. There was remarkably good compensation of the circulation following ligation of the inferior vena cava. The rate of water loss from the lower extremities determined on five patients eight days postoperatively was found to be normal."

In the last few years reports of cases in which vena cava ligation<sup>87, 88</sup> had been performed for phlebothrombosis have appeared in the American literature. All authors report good results with no postoperative sequelae and a minimal amount of edema, except Linton (quoted by Allen) who seemed disturbed by the fact that two of his patients showed postoperative edema and ulceration. We firmly believe that we have not seen these complications in the patients in whom we have ligated the vena cava because, in the earlier cases, we routinely blocked the lumbar sympathetic ganglia on either side postoperatively daily for four to five days, and in our later cases we sectioned the right and left sympathetic chains at the time of ligation.

Oehsner and DeBaKey<sup>62</sup> have shown that any trauma to a large blood vessel of an extremity throws the whole vascular bed into vasospasm, and that this spasm is responsible for some of the edema. Therefore, we believe that in ligation of vessels the size of the iliac or vena cava, the right and left lumbar sympathetic ganglia should be blocked routinely, or at the time of operation the lumbar sympathetic chains should be sectioned in order to relieve the spasm and minimize the possibility of untoward sequelae.

### Discussion

The complications arising from intravascular clotting in gynecologic and obstetric practice have been reviewed. To prevent these complications it is necessary that the patient be brought to the operating or delivery room in the best possible condition. Focal infection should have been removed, dehydration and demineralization combated, anemia eliminated by means of blood transfusions and hemopoietic stimulants, circulatory collapse and chilling prevented, abdominal distention minimized, and any interference with full respiration and any mechanical retardation of the venous return flow, such as pillows under the knee and perineal lights which involve flexion of the knee over holders, eliminated. Patients with varicosities should have their legs



In our series (Table III), palpable thrombosed vaginal or pelvic veins were found on vaginal examination in only 36 per cent of the cases, whereas at the time of operation, inspection and palpation of the pelvic viscera disclosed palpable and visible thrombotic veins in all cases but one. Chills were present in every case of suppurative pelvic thrombophlebitis, and, as was expected, chills were not observed in the two cases of pelvic vein phlebothrombosis, nor did the latter show any marked temperature rise, whereas, in the former group, all had temperatures ranging from 103° to 105° F.

Pulmonary infarction was not present in the two cases of phlebothrombosis, but was present in all but one of the cases of suppurative pelvic thrombophlebitis, and in four instances could be classified as massive. In addition to the cases herein reported, there have been four more patients who had ligation of the vena cava and ovarian vein for septic pelvic thrombophlebitis performed by another member<sup>83</sup> of the Department of Gynecology, Tulane University, during the period of January, 1943, to January, 1946, with resulting complete recovery. These four cases and Cases 11 and 12 of this series were not seen by us (on military leave), but are added to our personal series to complete the study of all cases of ligation of vena cava and ovarian veins performed by members of the Tulane Gynecologic Department, and thus better evaluate the efficiency of the procedure and present an uncorrected series.

There were no deaths in the cases in which the procedure was performed for phlebothrombosis or suppurative thrombophlebitis of the pelvic veins following gynecologic operations (Cases 1, 2, 3). The uncorrected mortality rate for all cases in which the procedure was performed for puerperal suppurative pelvic thrombophlebitis is 13.3 per cent (Table III). There were two deaths (Cases 6 and 12). In one the patient was practically moribund when operated on, and the thrombus extended from the left ovarian vein into the renal vein. At autopsy, it was found to continue into the inferior vena cava and superior vena cava ending in a core in the auricle of the heart. In addition, the patient had peritonitis at the time of operation (Case 6). The second death followed the operation by six days, and at autopsy the patient was found to have multiple embolic abscesses of the kidney, spleen, and lung. It is interesting to note that this patient was treated with penicillin and sulfonamides preoperatively, and probably the operation was performed too late (Case 12). Patients 13 and 14 were also operated on later in the disease than the cases seen prior to the author's entry into military service (1942), as we wished to give the patient every chance to recover by conservative measures and evaluate large doses of penicillin. These two patients did not respond, and ligation was performed. In Case 13, the thrombus in the left ovarian vein reached to within 4 mm. of the renal vein, but we were able to ligate proximal to it. We almost waited too long in this instance. In Case 14 the same trial of penicillin was given, and we procrastinated longer than our surgical judgment deemed it wise. The patient recovered, but now has an active endocardial lesion which we believe might have been prevented had we operated earlier, when it became evident that penicillin and sulfonamides were not producing the desired result. This result is classed as good. All other cases in which we performed vena cava and ovarian vein ligation for phlebothrombosis or suppurative thrombophlebitis of the pelvic veins had excellent and, in most instances, dramatic results. In all cases sulfonamide and penicillin therapy was discontinued at operation.

Follow-up examinations have been performed regularly to the time of writing on all patients except three, who died from two to three years following vein ligations. In none could the procedure in any way be associated with death. In Case 10 death followed operation, being performed for a pulmonary condition initiated by the patient's original infarctions prior to oper-



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tightly wrapped in elastic bandage prior to operation or delivery. Postoperatively, the patient should be made to move the extremities, wiggle the toes, or perform bicycle exercises to the greatest degree possible and many times each day. Early, selected, controlled ambulation should be encouraged and, of course, operation or delivery should be as aseptic, hemostatic, and atraumatic as possible.

### Conclusions

1. By simple preoperative and postoperative measures, the incidence of intravascular clotting, either aseptic or septic, can be lowered, and in this way a number of deaths and disabling and disfiguring sequelae can be prevented.

2. The routine postoperative or postpartal examination of the patient's legs is as important as examination of the abdomen. No complaint of thoracic pain, pain in the leg, or swelling of the leg should be casually dismissed.

3. Cases of pelvic tumors with unilateral or bilateral edema of the legs should be considered as having phlebothrombosis of the deep veins of the extremity or pelvis until otherwise proved. One should be careful about ascribing the edema or swelling to pressure produced by the growing tumor. In all cases in which phlebothrombosis or thrombophlebitis is found to be the etiologic factor, adequate therapeutic measures should be instituted prior to surgical attack on the abdominal tumor.

4. In cases of suppurative pelvic thrombophlebitis failing to respond to conservative measures, and especially those in which infarction has occurred, surgical therapy should be instituted.

5. If surgical therapy is instituted, the return flow of the blood from the uterus should be ligated, i.e., ligation of the vena cava and both ovarian veins.

6. Ligation of the vena cava and ovarian veins will save a number of lives, and the complications following this procedure are slight, if any.

7. Following ligation of the vena cava, the chances of postoperative complications can be minimized if the patient has routine postoperative lumbar sympathetic blocks, or if the sympathetic lumbar chain is interrupted at the time of operation.

8. Although the death rate from puerperal sepsis throughout the country has been materially lowered since the advent of chemotherapy and antibiotics, sepsis is still a major factor in the production of maternal mortality.

9. It is hoped that with the advent of newer chemotherapeutic agents and antibiotics, by legislation directed against abortionists and by education of the public and physicians, some day we will be able to report not on how many patients died of puerperal sepsis or survived puerperal sepsis as a result of conservative or surgical therapy, but that we no longer see this dreaded complication on our service.

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Our therapy is simple, never surgical. Gynecologists are well aware that many patients are predisposed to phlebothrombosis and thrombophlebitis. Surely, all of these should have preoperative determination of prothrombin activity and coagulation time, as well as other prophylactic care. And I believe the time is near at hand when selected cases among this group of patients will be protected by preoperative prophylactic prothrombin-controlled dicoumarol therapy in small amounts, e.g., not over 100 mg. daily for one or two days.

All cases on our service with inexplicable postoperative fever, rapid pulse, chest pain, or other intangible symptoms indicative of possible phlebitis or embolism are given 100 mg. of dicoumarol immediately, this medication repeated daily under prothrombin control if the symptoms persist.

In cases with more definitely suggestive early evidence indicative of thrombophlebitis we give also one-half ampule (50 mg.) of heparin, intravenously, two or three times each twenty-four hours until repeated determinations of prothrombin activity reveal that a 100 mg. daily dose of dicoumarol has become effective. When used for prophylaxis, we give no more than 100 mg. of dicoumarol daily, and endeavor never to reduce the prothrombin time below 50 per cent.

Under a regimen as outlined, definite acute thrombosis is infrequent. In the event of its occurrence, our routine is that commonly advocated—heparin intravenously every four hours until daily administration of conservative amounts of dicoumarol becomes effective, penicillin and sulfonamides in the presence of infection, local care of the affected part, forced fluids, free elimination and early ambulation.

I have no views relative to the efficacy of venous ligations in contrast with measures previously employed. Heparin and dicoumarol therapy, one or the other, or both, is more simple, more safe and, I believe, more satisfactory.

DR. JAMES C. MASSON, Rochester, Minn.—With few exceptions, the discussions of other papers on this program have been more or less in accord with the views of the essayist and I am sorry to raise a discordant note at this time. My views are radically different from those just presented.

To begin with, I think that all venous clotting starts as a so-called phlebothrombus and it is not until the vessel is occluded and clinical change takes place in the thrombus and stagnated blood that elevation of temperature, pain, tenderness and swelling make the diagnosis of thrombophlebitis possible. In my experience, most of the fatal pulmonary emboli occur with little or no previous warning. Most fatal pulmonary emboli, on the other hand, may result from small floating thrombi or from small proximal extensions from a fixed thrombus and they may occur from above a ligature. In my experience it has been difficult to decide when and what veins should be ligated to protect against pulmonary embolism, and I think the promiscuous ligation of major veins as a prophylactic measure is not warranted, especially in view of the possible sequelae that may be a definite handicap to the patient in future years. Furthermore, ligation of any veins above the common femoral must be considered a major procedure on an already sick patient.

Parasympathetic lumbar blocking with a local anesthetic is an efficient and valuable method of causing vasal dilatation with relief of pain and reduction of lymphedema. In the case of a very sick, frightened patient under tension this procedure is looked on at least as a minor operation; furthermore, I think that much the same results can be obtained by properly applied heat and proper elevation in a sling with suspension from above the bed. In patients in good condition, the addition of whisky by mouth has some vasodilating effect, and tends to relieve tension and improve morale rather than frightening and depressing the patient.

I do not feel that ligation of a major vein should be considered lightly. I have only once ligated the left common iliac vein. It is now one and a half years since the operation and the patient is definitely handicapped and uncomfortable with a large swollen leg. I have not had experience with definite infection in veins such as occurs in cases of puerperal infection. In such cases ligation above the infected thrombus as advised by Dr. Collins might well be a lifesaving measure. On the other hand, a thrombus or embolus starting in the

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1430 TULANE AVENUE

### Discussion on Papers of Dr. Meigs and Dr. Collins

DR. ARTHUR H. CURTIS, Chicago, Ill.—As a preliminary, I wish to call your attention to the fact that Dr. Collins' statistics indicate that the thrombophlebotic syndrome has occurred in not more than one in 1,000 cases on his service.

I am in accord with Dr. Collins and Dr. Meigs in their emphasis of the need for watchfulness in recognition of the earliest evidence of acute thrombosis. Elicitation of tenderness in the calf of the leg is important presumptive evidence of a venous lesion; it rivals a positive Homans' sign in the diagnosis of a thrombotic process.

Meigs' procedure of comparative mensuration of the legs, after marking with ink a prescribed distance above and below the patella, is an ingenious contribution.

I also agree with the essentials of the prophylaxis recommended against development of the thromboembolic syndrome. Prophylactic postoperative passive exercise of the legs is part of our routine. We also encourage all patients to move about freely in bed, but no specific exercises are ordered. I have always believed that pillows under the knees "jack-knife" the patient and are harmful; unfortunately, it is a favorite with nurses and with patients.

Early ambulation has never appealed to me. It has always been our rule to permit patients to get out of bed as soon as they feel disposed to do so, but I am opposed to forced early mobilization; it may reduce the incidence of thrombosis, but I am convinced that it increases materially the amount of permanent postoperative discomfort.

It is amazing to me that bilateral femoral vein ligation has become so popular with men of eminence in our profession. It is almost beyond belief that Dr. Collins has become an enthusiast over venous ligation in puerperal sepsis and that it has appeared necessary to perform ligations in so many of the gynecologic patients operated on during the last five years at the Massachusetts General Hospital at a time when the efficacy of heparin and dicoumarol has already been demonstrated.

In the May 18 issue of the *Journal of the American Medical Association* is a report from the Mariestad Hospital, Sweden, on the intravenous heparin treatment of 209 cases of acute thrombosis among 16,495 admissions during the last five years. The number of operations was about 7,000, without a single postoperative death from thrombosis or embolism. There was a total mortality of three cases from pulmonary embolism among the nonoperated group. One of these received no heparin, one had only one injection before death, and the third patient had far advanced thrombosis on admission. In contrast with these three fatal cases, there were 47 deaths from embolism during the preceding five-year period, when heparin was not available.

DR. LEWIS C. SCHEFFEY.—Philadelphia, Pa.—During the past five years, we have become very alert in trying to differentiate between phlebothrombosis and thrombophlebitis, and the implications concerned with them, on the Obstetrical and Gynecological Service at Jefferson Medical College Hospital.

One of the things that has been stressed is the education of our house men in recognizing these conditions. There has been close cooperation between our department and general surgery. We have instituted a broad prophylactic program with which our staff members, residents and interns have become familiar.

The necessity of active motion postoperatively, deep breathing, avoidance of cramped positions and pillows under the knees, avoidance of distention, and early rising as soon as agreeable after operation, is stressed constantly.

In addition, the house staff has been instructed to check the condition of the extremities daily, and carefully to evaluate any and all complaints of pain or distress that might possibly be significant. We endeavor to distinguish between thrombophlebitis and phlebothrombosis on the basis of respective symptoms and physical signs, for our management of these conditions differs distinctly.

*Thrombophlebitis.*—Here we have relied entirely upon the sympathetic block and in no case per se has Dr. Willauer, the surgical consultant urged the ligation of the femoral vein. Pain in the groin, medial aspect of the thigh or buttock, particularly when preceded by an unexplained fever or rapid pulse, suggest thrombophlebitis. Examination shows perhaps some abdominal distention, with tenderness over the femoral vein or groin. The foot of the affected limb or limbs may be cold and/or moist, though color may be normal. There may be edema of varying degree.

For such a symptom complex we elevate the foot of the bed about eight inches, keeping the patient flat, but moving about actively and encouraging pulmonary ventilation. Light dressings are changed, water balance is checked and corrected if indicated.

Lumbar sympathetic nerve block (with eucupin-procaine solution) is carried out promptly if symptoms and signs continue to progress, but if coldness and moisture of the affected part or parts predominates, continuous spinal anesthesia at the 5th or 6th thoracic segment is given for two to three hours, instead of sympathetic block.

No ligations of any of the femoral or pelvic veins have been done in these cases of thrombophlebitis, nor have there been any *discovered* embolic phenomena, and no deaths from embolism with this regime of treatment.

*Phlebothrombosis.*—Here the symptoms are slighter and much more vague, but indicative of a graver and more serious situation. Usually afebrile, an ache in the foot or calf of leg is significant; also the feet may feel tender to the patient. On examination there may be slight swelling about the ankle or lower leg, with a degree of cyanosis perhaps. On the affected side the foot cannot be flexed with the same ease as on the opposite side. Homan's sign is present, tensing of the Achilles tendon causes pain in the calf or back of the knee. No signs are usually present in the thigh. Pulsation of the dorsalis pedis and the posterior tibial arteries may differ comparatively in the affected leg, being almost imperceptible or even absent.

With the above findings, we immediately carry out ligation and division of the superficial femoral vein below the profunda femoris, with removal of all clots so that a retrograde flow may be obtained. If this does not happen, then ligation at higher levels in the pelvis is done (with local or spinal anesthesia). Patient becomes ambulatory at once or as soon thereafter as possible. We have not as yet performed prophylactic femoral ligation in our patients. There have been no embolic phenomena and no embolic deaths since carrying out this form of management.

DR. COLLINS (Closing).—In answer to Dr. Curtis, the figures we gave of the number of involved veins with infection—9.3 per cent—were uncorrected. The figures were not compiled from the number of autopsies, but from the whole series of deaths, the figure being uncorrected. The correct figure in the patients dying from septicemia is 35 per cent showing involvement of the veins; which figure closely approximates those from other parts of the country.

deep veins in the leg is *never*—and I repeat, in my experience, *never*—infected and the name “thrombophlebitis” is misleading. Repeated cultures from clots and walls of veins are always negative. The elevation of temperature, pain, tenderness, lymphedema, etc., are the result of clinical changes in the clot and stagnated blood with an influx of leucocytes and of vasospasm with resulting lymphedema. This condition must be distinguished from septic thrombophlebitis. It has not been at all uncommon in my experience to find thrombosed veins in the bases of the broad ligaments in the course of a pelvic operation, and I have so far never had cause to regret not doing a prophylactic ligation of a major vein proximal to the clot.

Anticoagulants (heparin and dicoumarin) are being used in the Mayo Clinic in cases of nonfatal pulmonary embolism and on at least one service dicoumarin is used prophylactically in all cases in which there is a high tendency toward thrombus.

In the last four years (1942, 1943, 1944, 1945), with ten surgeons operating, hysterectomy has been performed 4,810 times with 26 occurrences of diagnosed pulmonary embolism but only six deaths or 0.1 per cent.

My own service with a fair share of the more difficult cases can be looked on somewhat as a control, as I do not use anticoagulants. In the same four years, I did total abdominal hysterectomy in 709 cases with only two deaths. The cause of one death was diagnosed as pulmonary embolism but there was no necropsy and the cause may have been cardiac. The other death was from peritonitis. In only one other case was pulmonary embolism diagnosed and in that case pleurisy was present. The patient made a good recovery. In the same years, 1942 through 1945, I did vaginal hysterectomy in 413 cases with two cases of pulmonary embolism. Only one patient who had pulmonary embolism died, a mortality rate of 0.2 per cent from pulmonary embolism. During the last two and a half years, that is up to the present time, I have done abdominal hysterectomy in about 400 cases. There have been no deaths from any cause and no major veins have been ligated.

In closing, I do not want to pass judgment on a method with which I have had practically no personal experience. My own reaction is that I do not see many cases in which prophylactic ligation of veins is required. Furthermore, I know that in some clinics, like the Lahey Clinic in Boston, where formerly such procedures were used in a considerable number of cases, they are now almost entirely disused.

It is hard for me to believe that in my series quoted previously, with an over-all mortality rate of 0.3 per cent and a mortality rate from pulmonary embolism of 0.1 per cent, prophylactic ligation of veins was indicated.

DR. E. L. KING, New Orleans, La.—I worked with the late Dr. C. Jeff Miller for many years and, as you probably all know, he did ligation of the veins in some of these cases. We had considerable experience with suppurative thrombophlebitis, especially at the Charity Hospital where we have many cases of septic abortion. I think we should emphasize that we are fearing not only pulmonary embolism, but spread of the infection through the system and multiple infections elsewhere, in addition to the embolism.

I have had one case of vein ligation in consultation, a patient that had been badly handled. In that case we did ligate the vena cava and did a hysterectomy. The patient recovered and had no trouble whatever so far as the swelling or circulatory condition of the leg was concerned. We do believe it is indicated in these particular cases, shown clinically more than anything else by the high temperature and chills. It is a definite picture, a clinical entity and the condition seems to be best handled by ligation.

DR. CURTIS (in reply to Dr. E. L. King's discussion).—It is my very definite impression that Dr. Miller ligated the veins in puerperal sepsis, in a few instances experimentally, and made up his mind that it was not a valuable or indicated procedure.

DR. KING (continuing).—Dr. Miller changed his mind very frequently, I may say. He would ligate the veins and get very good results; then in some others he would not get such good results. Perhaps he did not go high enough in those latter cases. In the later years he did ligate more often, always the hypogastriacs and the ovarians.

## ON THE ORIGIN OF CERTAIN PERISALPINGEAL CYSTS\*†

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**S**MALL cysts of varying size are found in the wall of the uterine tubes. The derivation of these cysts has received much attention, and there are many hypotheses to explain their origin. They are said to arise from the junctional system, the epoophoron, paroophoron, Kobelt's tubules, and the pronephros (hydatid of Morgagni) (Gilbert and Shorey<sup>1</sup>). An excellent review of this subject is given in the Stoeckels *Handbuch der Gynaekologie*.<sup>2</sup> The purpose of this communication is to draw attention to certain cell balls containing cystic structures, to discuss the possible origin of these structures, and to offer them as an additional starting point of pelvic adenocarcinoma.

Isolated accumulations of cellular elements forming small clumps or balls are frequently found in the wall of the uterine tubes. They are commonly situated in the outer portion of the tubes, just beneath their peritoneum. From the shape of the cells it seems clear that they are epithelial. They resemble those lining the lower urinary tract and should be classified as transitional epithelial cells.

Ten apparently normal uterine tubes were cut into several blocks and many random sections taken. Six tubes contained these cell balls.

The individual cells are round or oval-shaped, approaching spindle forms. They exhibit an eosinophilic or clear cytoplasm and clear-cut vesicular nuclei. The cells are densely packed, but their cellular membranes are always recognizable. They are surrounded by what appears to be a basal membrane. Such cell balls have been observed and described by various investigators, and their origin considered to be the same as that of the cystic structures previously mentioned.

On examination of a series of these cell balls, it was noted that a pinkish, homogeneous material often appears in the centers of these cell nests and that nuclei of adjacent cells become pale-staining or absent. It seems that the cells situated within the center tend to degenerate and liquify, forming small cystic structures. The cells forming the innermost lining of the cyst assume first, low cuboidal, and later, high cuboidal shapes, while the cells situated peripherally remain transitional in character. As such cysts enlarge, fewer transitional cells are found. These then become cystic structures lined by cuboidal cells with a few transitional cells present at only one pole of the cyst. In later stages when the pressure within the cyst has increased, the inner lining cells are found to be compressed and flattened, and resemble endothelial cells. Finally, all lining cells disappear and the cyst is lined by a thin membrane only.

\*Read (by invitation) at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

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As to the drugs mentioned, I have no experience with dicoumarol or heparin. Some investigators and clinicians do not think heparin and dicoumarol should be given in postabortal cases, especially where there is infarction of the lung associated with a septic process in the vein, as a number of those patients will die from hemorrhage from the lung as a result. Where a major vessel is ligated and not had immediate block there may not be any persistent edema. While that is true, I think one can minimize or reduce the number of cases of postoperative edema if section of the sympathetic chain is performed to increase the peripheral circulation, relieve the vasospasm and decrease the capillary anoxia.

DR. MEIGS (Closing).—I have recently been in New Orleans and have had the privilege of seeing two of Dr. Collins' patients and they have an absolutely perfect result, with no evidence of any swelling of the legs. I think that is due to the fact that he does not injure the circulation by tying off the vena cava because these patients have already a block of the vena cava. All he does is to prevent embolism and septic infarcts.

Dr. Collins is using a therapeutic ligation. Nature has taken care of the legs and Dr. Collins is preventing the patient from having septic infarcts, which I think is very commendable.

We must select cases for superficial femoral vein ligation. If a patient develops a mild thrombophlebitis, some will have an embolism. If you can ligate the superficial femoral veins, which is a simple procedure, without injury to the patient, it should be done. We have no swollen legs. In suspicious patients there is a rise of pulse, temperature and respiration, the "Allen sign." Dr. Allen feels that if the above occurs then the patient has had a small infarct, and the patient's veins should be ligated. If a patient has tenderness in the calf, something should be done about it. I am sure we all believe that if a patient has an infarct—and I think it would be the same with you if any of you developed an infarct after an operation—the femoral vein should be ligated.



cysts. His illustrations show that he was dealing with a type of cyst lined by transitional cell epithelium.

He believed that (1) they represent Wolffian duct rests, (2) they may be derived from the epithelium lining the coelom cavity rather than from suprarenal rests and, (3) they are produced by inflammation. A similar epithelium later forms the anterior wall of the sinus urogenitalis and the urinary bladder.



Fig. 1.—Urinary bladder. Note the small islets of transitional cells with central cyst formation. Also note the cuboidal appearance of the inner lining of the early cyst. (Iron-hematoxylin-eosin preparation). ( $\times 130$ ).

Fig. 2.—Urinary bladder. Cell balls with cyst formation. Note the cuboidal lining cells. (Iron-hematoxylin-eosin preparation). ( $\times 130$ ).

If it is true that these cell balls in the wall of the tube are epithelial in nature and are transitional epithelium similar to that lining the urinary bladder, one would expect that occasionally carcinomas might arise from these structures. Carcinomas of the urinary bladder are most commonly papillary transitional cell carcinomas. Only rarely are adenocarcinomas with transitional epithelial features encountered there. These are said, as stated before, to arise from the transitional epithelial cells of Limbeck and Brunn.

Sometimes the presence of both transitional and cuboidal cells can be observed in a single uterine tube.

These cell balls and cystic structures call to mind the so-called cell nests of Limbeck<sup>3</sup> and Brunn.<sup>4</sup> Such cell balls have often been observed beneath the mucosa of the urinary bladder, the ureter, and more rarely, the pelvis of the kidneys. They constitute circumscribed accumulations of transitional cells. The centers of these cell balls occasionally show cystic degeneration. When these cystic structures project over the mucosa, they give rise to the so-called cystic cystitis.

Saphir and Kurland,<sup>5</sup> who had studied several such instances, described the gradual changes from transitional to cuboidal cells forming the inner lining of such cystic areas. Furthermore, they have traced the origin of rare adenocarcinomas arising in the urinary bladder to the cuboidal cells lining such cystic areas. The change from transitional cells to cuboidal cells was explained as a reversion to an embryologically younger form of epithelium, and taken as an example of so-called de-differentiation. It has often been stated that as a result of inflammation, regeneration, or tumor growth, new cells undergo a de-differentiation or reversionary process in the direction of the primary embryonal or blastomere cell. With further growth there is a re-differentiation to form a type of cell not identical with the original type. This new differentiation produces cells of a lower order of specialization than the original, but may occasionally progress higher. This is progressive or prosoplastic metaplasia (Karsner).<sup>6</sup> Pinesohn<sup>7</sup> pointed out that the columnar epithelium in the bladder developed by means of "indirect" metaplasia. He considered that the dominant cell type of a tissue may become inferior to the recessive cell type which in turn becomes dominant.

The bladder develops from the cloaca which is lined by cylindrical epithelium. This epithelium is dominant in the rectum, inferior and recessive in the bladder, where the transitional cell epithelium is dominant. Any irritation may be the cause of epithelial proliferation or regeneration. The epithelium now may become atypical and the transitional cell revert to an inferior recessive type, while the inert inferior recessive type, the cylindrical cell, becomes dominant. Thus, cylindrical cells are seen. Within the cell nests of Limbeck and Brunn it is apparently the cystic degeneration which causes the de-differentiation.

It is, of course, hazardous to conclude similarity of origin from the fact that structures closely resemble each other morphologically, i.e., the cell balls in the urinary bladder and those within the wall of the uterine tubes. However, the cells of both types of cell masses seem similar histologically. Furthermore, it is significant that the innermost cells lining degenerated cystic areas become cuboidal in both instances. It seems possible that some of the lining cells of the cloaca are misplaced along the Müllerian duct, and there change to transitional cells just as those in the normal urinary tract mucosa. Whenever degeneration with cyst formation occurs in cells which are separated from the normal urinary tract mucosa, as in the cell nests of Brunn and Limbeck and those described in the wall of the tubes, the cells adjacent to the cystic, degenerated areas revert to the embryologically younger form of epithelium. It may be mentioned here that as early as 1904, Robert Meyer<sup>8</sup> studied such epithelial

The right tube was a dark, reddish blue, tubular structure, measuring 20 cm. in length. It was markedly dilated and presented several kinks. Its external surface was glistening and contained minute blebs. The smooth distal fimbriated end of the tube measured 8.5 cm. in diameter. A pale, gray-pink tumor of semi-firm consistency protruded from the tubal surface. This tumor measured 6 by 8 cm. in its greatest dimensions and was covered by tubal serosa.



Fig. 5.—Small cell balls in wall of tube. Note cystic degeneration in center, and the cuboidal appearance of the cells lining the cyst. (Iron-hematoxylin-eosin preparation.) ( $\times 130$ .)

Fig. 6.—Wall of tube. Note the cell ball with cystic degeneration, and low cuboidal type of cells lining the cyst. (Iron-hematoxylin-eosin preparation.) ( $\times 240$ .)

On section, it was seen that it arose in the wall of the tube, and secondarily invaded the mucosa and extended into the lumen of the tube. The tumor was of a greyish pink color, finely granular, with foci of necrosis and hemorrhage. The tube contained much serosanguineous material. The ovaries and the left tube showed no significant changes.

On histologic examination, it was found that the tumor consisted of epithelial cells which, though varying in size, were principally elongated or slightly oval, with oval, vesicular nuclei (Figs. 11 and 12). Atypical mitotic figures were abundant. There were many small blood vessels present, and the tumor cells seemed to be closely attached to the vessel peripheries. In some fields the formation of cores of an insignificant amount of connective tissue with one or two

Two instances of carcinoma which seem to have arisen from the transitional epithelial balls of the uterine tube were recently found.

CASE 1.—An uncomplicated transitional cell carcinoma was found in a 47-year-old woman admitted to the private Service of Dr. William H. Rubovits because of uterine bleeding. There was no tumor palpable at that time. A vaginal hysterectomy was performed. During the operation, the tubes and



Fig. 3.—Urinary bladder. Cell nests with small cyst. (Hematoxylin-eosin preparation). ( $\times 130$ ).

Fig. 4.—Large cell ball in wall of tube. Note the transitional cells which make up the cell ball. (Iron-hematoxylin-eosin preparation). ( $\times 90$ ).

ovaries were inspected and palpated, and were found to be normal. Histologic examination of the uterus showed a hyperplastic endometrium with early fibrotic changes. There were several polyps present and also an old cervical erosion. This patient was re-admitted eleven months later complaining of pain in the right lower quadrant. Bimanual examination revealed a palpable mass in the right pelvis. Laparotomy was performed, and both ovaries and tubes were removed.

may be confused with the spindle-cell sarcomas and lead to the erroneous diagnosis of carcinosarcoma. At any rate, adenocarcinomatous structures and transitional cell carcinomatous structures are occasionally encountered side by side in such tumors. It is of interest to note that similar tumors consisting of adenocarcinomatous structures and transitional epithelial cells also occur in the urinary bladder. These tumors, as stated above, are thought to arise from the

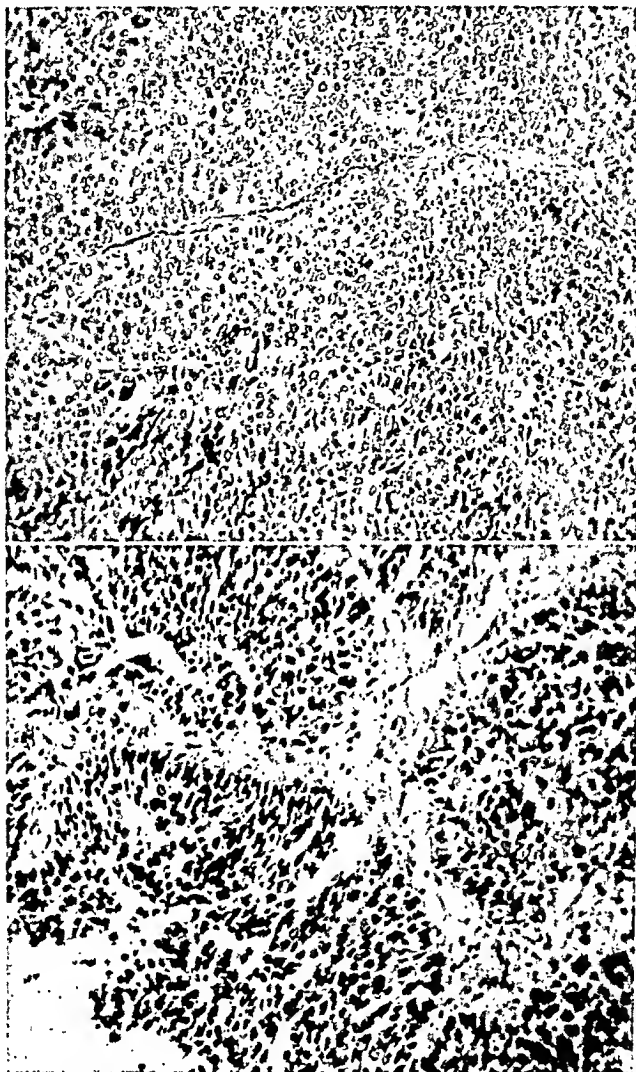


Fig. 9.—Section of primary tumor of the Fallopian tube. Note the transitional type of tumor cells and their relation to the thin walled blood vessel. (Hematoxylin-eosin preparation). ( $\times 110$ ).

Fig. 10.—Section of primary tumor of the Fallopian tube. Note the transitional type of tumor cells simulating those seen in the urinary bladder. (Iron-hematoxylin-eosin preparation). ( $\times 130$ ).

cell nests of Limbeck and Brunn. From this study, and also from studies of instances of adenocarcinomas of the urinary bladder, the origin of adenocarcinomas with transitional carcinomatous structures from cystic degenerated cell nests of the wall of the tubes must be considered.

CASE 2.—The second patient had a primary tumor involving the entire left pelvic region. At first it was thought to have originated within the left ovary. It was found in a 53-year-old patient, who had had a hysterectomy thirteen

small vessels was noted. Some of the cores with the adjacent tumor cells seemed to form smaller or larger papillary structures. From the appearance of the tumor cells it was concluded that they were transitional epithelial cells, similar to those seen in tumors arising from the mucosa of the urinary bladder. It was obvious that this tumor did not constitute a metastatic growth. The origin seemed to be the transitional epithelial cell balls in the wall of the tube.



Fig. 7.—Wall of tube with transitional cell balls and cyst formation. Some of the lining cells are flattened, resembling endothelial cells; others still are of low cuboidal type. (Iron-hematoxylin-eosin preparation). ( $\times 130$ ).

Fig. 8.—Wall of tube with cystic cell ball. The lining cells in the right lower field are compressed, resembling endothelial cells. Cuboidal cells are still recognized forming the innermost lining of the cyst at the left. (Iron-hematoxylin-eosin preparation). ( $\times 130$ ).

Often, adenocarcinomas are found in the pelvis with complete destruction of one ovary and tumor formation within the pelvic peritoneum, broad ligament, and wall of the tubes. In the absence of any other primary site of the carcinoma, it is usually assumed that the primary carcinoma is located within the ovary. Sometimes, papilliferous and adenocarcinomas are found, in addition to diffusely infiltrating carcinoma cells which seem of the transitional type. It has been pointed out that in these latter instances, when the transitional cells invade the core and the ovarian structures, they often assume spindle shapes. Such tumors

Adenocarcinomas of the urinary bladder are thought to arise from the cell nests of Limbeck and Brunn. In addition, they may arise from the cells adjacent to the cystic degenerated areas of these cell balls in instances of cystitis cystica if transitional carcinomatous structures are present, in addition to malignant glandular structures.

In the same way, the presence of degenerated cell balls and malignant glandular structures within the uterine tubal wall would tend to support the theory that this type of mixed malignancy may arise from nests of epithelial cells which originate from the lower urinary tract epithelium.

### Summary

Attention is drawn to cell balls which are often encountered in the wall of the uterine tubes. These consist of transitional cells and very closely resemble morphologically those described by Limbeck and Brunn in the urinary tract. The cells in the center of these balls often become liquified and form cysts.

The cells forming the inner walls of such cystic, degenerated areas assume cuboidal shape. The origin of adenocarcinomas in the urinary bladder is traced back to these cystic, degenerated cell balls. Changes similar to those occurring within the cell balls in the urinary tract have been observed in the cell balls located in the wall of the tubes, including the change into cuboidal cells. Because of the resemblance of these cell balls to those described by Limbeck and Brunn, because of the close resemblance of the individual cells of these nests to the transitional cells lining the urinary tract, and because of the similarity in morphologic alteration of the cells lining the cystic degenerated areas, it is suggested that these cell balls and cysts seen so often in the wall of the tubes may arise from misplaced lower urinary tract epithelium.

A primary papillary transitional cell carcinoma of the uterine tube is recorded. This probably took its origin from such epithelial cell balls. A second carcinoma involving both the tube and the ovary is described. This tumor consisted of both transitional epithelial features and glandular structures. It is possible that this tumor may also have arisen from such cell balls of the tubal wall.

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### Discussion

DR. JOHN L. BREWER, Chicago, Ill.—These tumors that arise in the Fallopian tubes are rare, and, as such, one person does not have access to a great amount of material. The conclusions that can be gained from a study of such tumors is further complicated



years before. She developed a mass in the left lower quadrant with marked ascites, had continuous fever, severe abdominal pain, became progressively and rapidly weaker, and died.

At autopsy the region of the left ovary was completely replaced by a tumor mass which was partly firm, gray, and presented a finely granular, partly cystic, cut surface. The left tube and broad ligament could not be clearly identified. The right ovary was enlarged and the seat of a metastatic tumor. Metastases were found in the peritoneum, liver, and sigmoid colon.

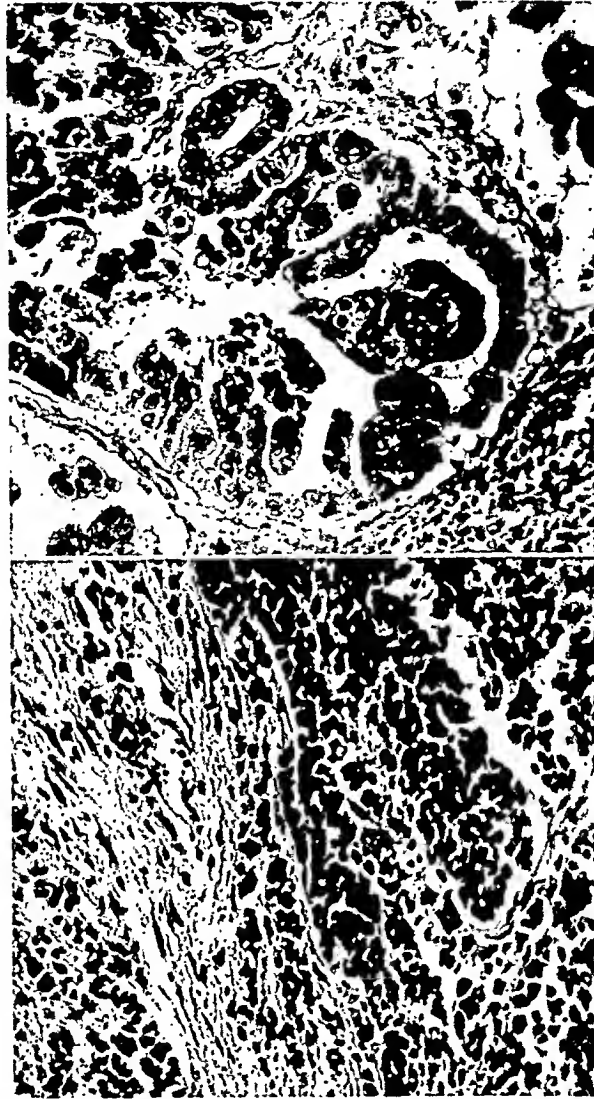


Fig. 11.—Adenocarcinomatous structures in tumor found in the region of the ovary. (Iron-hematoxylin-eosin preparation.) ( $\times 130$ .)

Fig. 12.—Section taken from the same tumor as shown in Fig. 11. Note the transitional type of tumor cells. (Iron-hematoxylin-eosin preparation.) ( $\times 130$ .)

Histologically, the tumor consisted of large masses of epithelial cells (Figs. 9 and 10). Many of them were spindle or oval shaped with vesicular nuclei that varied much in size, shape, and staining quality. There were also distinct glandular structures lined by cuboidal cells which disclosed evidence of malignancy. Both of these malignant structures were found in the primary tumor and in the metastatic growths. A diagnosis of primary adenocarcinoma of the ovary with marked anaplasia cannot be ruled out completely, but it might be possible that this tumor arose from transitional cell balls of the left tube.



DR. EMIL NOVAK, Baltimore, Md.—It is difficult to evaluate Dr. Reis' paper on the mere basis of the lantern slides which he has shown, but I would have the impression that the cell nests which he has described, and from which he believes that certain cysts arise, are to be classed as Walthard islets. The latter most often appear as ovoid plaques of squamous epithelium, but they may at times be of glandular appearance. They are found more often on the tube than on the ovary. Another picture is also encountered on or near the ovarian surface which may be confused with Walthard islets. Under the influence of inflammation, marked peritoneal metaplasia may occur, with at times a heavy stratification of the cells, so that the lesion may look like a Walthard cell nest with cystic central degeneration.

So far as I know, the Walthard islets have not been suspected of giving rise to cysts, other than the occasional pseudomucinous cysts which may arise as a result of the pseudomucinous metaplasia of the Walthard epithelium which sometimes occurs. It is the Brenner tumor which is believed to have its origin from Walthard islets. Further evidence to support this view has recently been furnished by Danforth and by Ayers, who showed that the epithelial cells of Brenner tumors, and those of Walthard rests, often show an identical longitudinal coffee-bean-like grooving.

While it is not difficult to believe that certain bladder tumors arise from gland elements of urogenital origin, a similar explanation for periovarian or peritubal cysts seems to me a bit more difficult to accept, because of embryologic considerations which it would be difficult to discuss in the few seconds left me of my allotted time.

DR. REIS (Closing).—The Walthard nests seem to me to consist of squamous cells with no definite cell membrane, with pale, nonvascular nuclei that often were pyknotic. None of these I have shown today has a clearly marked cell boundary, and there was no change in configuration which would make any of them coffee-bean in appearance as in the Walthard cell nests or the Brenner tumors. My experience with Brenner tumors has been very limited, but those that I have seen have had a fibrotic network with these masses of cells in the center. They are large, their nuclei pale, and in none of them were we able to demonstrate any cell membrane. While they may be related to Brenner tumors, I think some of them have been included erroneously.

I cannot presume to debate embryology with Dr. Novak, but I had the concept that possibly, as this epithelium grew upward to meet the downgoing urinary tract from above, some of these cells might have wandered just enough laterally to have been included in the downgrowth of the Müllerian duct, and might have remained over.

by the fact that many are of such size that the determination of their source of origin is impossible. Apparently, there does occur in the tube certain tumors which have transitional character epithelium, and also some having an associated adenocarcinoma.

The author has suggested a possible origin of transitional cell carcinoma and adenocarcinoma of the Fallopian tube. This thesis logically followed the work done by Saphir and Kurland, in which they traced the origin of adenocarcinoma associated with transitional cell carcinomas from cell nests in the urinary bladder. The author has demonstrated a similarity between these cell nests of the bladder and cell nests found in the Fallopian tube wall. Several questions are immediately posed concerning these cell masses. The first is that concerning their origin. The author believes that they arise from cloacal epithelium. There are different opinions regarding the origin of the cell nests along the tissues of the urinary tract. The most prevalent theory is that they arise as a result of localized inflammatory reactions. There is evidence that this latter statement is true for the cell nests in the bladder, and it has also been suggested for the cell nests in the tube. From the tissues that I have observed, however, a striking feature is the absence of any evidence of inflammatory reaction in association with the tubal cell nests. The only evidence that I know of that the cell nests of the tube originate from cloacal epithelium is that which the author presents, and which is based upon the histologic similarity of the two groups of cell nests. More conclusive evidence is required before the origin can be definitely stated.

Second, the cuboidal and columnar epithelium found in association with the cell nests in the tube is similar in appearance and relationship to that seen in the cell nests in the urinary bladder. This has led the author to believe more strongly that the two groups of cell nests are identical. The relationship of the cell types also offers a possible explanation for the occurrence of adenocarcinoma and transitional cell carcinoma in the same tumor in both the tube and urinary bladder. The cell stages in transition to the malignant tumor formation in the bladder has been traced, but in the specimens presented in this paper such transitional stages are not seen. Again, however, the similarity of the malignant tumor tissue in the two locations suggests the possibility of their similar origin. Proof, however, cannot be established until transition from the cell nest tissue to malignant tumor tissue in the tube has been demonstrated. The author realizes this and has offered this suggestion, and only because there is as yet no established proof of the origin of these tumor types in the Fallopian tube.

There are a few questions that I would like to ask:

1. Since the tumor described originated in that portion of the tube at the mesosalpinx attachment, I would like to ask if any of the benign cell nests were found in any specimens in a similar location? In those specimens that I have observed, the cell nests are uniformly just beneath the serosa around the periphery of the tube and are not found in the mesosalpinx attachment region.

2. Are these cell nests described by the author the same as the cell groups to which the name Walthard cell nests is given?

The suggested idea of this paper deserves consideration and future efforts should be directed toward a study of the potentialities of these cell masses.

DR. JAMES R. MILLER, Hartford, Conn.—I have read the literature mentioned by Dr. Reis with great interest, for it leads me down paths which I had not previously explored. We have noted these cell balls and have observed this tendency to cyst formation. I have examined carefully the six cases of carcinoma of the tube which we have had at the Hartford Hospital, four of which have been my own, and have studied briefly nine others which Dr. Gordon Douglass kindly allowed me to review at the New York Hospital. A study of these slides leaves me with an open mind as to the possibility which Dr. Reis has suggested, but that is by no means saying that I could find many suggestions from the tubal carcinomas that would lead me to suspect the etiology in Lubeck and Brunn cell balls. Perhaps a very early specimen of tubal carcinoma may turn up which will help to decide this question. The transition which has been observed in the case of adenocarcinoma of the bladder is needed before this thesis can be considered as proved.

mental and functional failure may occur which will make any functional salvage minimal. Nevertheless, each patient in this group merits careful consideration and evaluation of her anatomic and physiologic assets in order to exclude disease and to select the occasional patient who may benefit from treatment.

*Group 2. Amenorrhea Associated With Tumors (7 patients).*—Seven patients were found to have amenorrhea associated with the presence of tumors. Four of the tumors were located in the pituitary, one in the floor of the fourth ventricle, and two in an adrenal gland. This group of patients is small but important. Two of the seven had never menstruated and had previously received treatment for the amenorrhea; one of these was found to have a glioma on the floor of the fourth ventricle, and the other a chromophobe adenoma of the anterior lobe of the pituitary gland. These two patients did not present general or neurologic symptoms, and the lesion was evident only on roentgenographic examination. One of the total of seven patients had been treated for postpartum amenorrhea when 22 years of age. When she was seen at the clinic a year later, examination revealed a tumor of the left adrenal gland. This patient, no doubt, had little to suggest such a diagnosis early in the course of the amenorrhea, but when seen by us she presented a typical picture of Cushing's syndrome, and later died of metastasis.

These cases serve to emphasize the necessity of complete examination when a young woman presents herself with established amenorrhea. Chromophobe tumors of the pituitary and suprasellar lesions often are not associated with signs of disease of the nervous system early in their development. Assays of the amounts of hormone substances in the blood and urine will reveal the same evidence of failure of function that may occur without organic disease. The somatic changes evident in the presence of basophilie and eosinophilie adenomas of the anterior lobe of the pituitary are absent in those patients who have chromophobe adenomas and suprasellar tumors. The latter lesions interfere with the function of the anterior lobe by compression of the functioning part of the gland and not by primary alteration of function due to the new growth. The early diagnosis of the chromophobe and suprasellar tumors is often made only by roentgenograms of the sella turcica.

*Group 3. Amenorrhea Associated With Anorexia Nervosa (15 patients).*—Fifteen patients experienced amenorrhea in association with anorexia nervosa. Naturally, variation exists in the amount of inanition and functional failure of the pituitary and ovary in these patients. In our experience at the clinic, approximately 50 per cent of young women suffering from anorexia nervosa have associated amenorrhea.

The average weight of this group of 15 patients was 86 pounds (39.0 kg.); the least weight was 61 pounds (27.7 kg.); and the greatest, 115 pounds (52.2 kg.). The average loss of weight was 40 pounds (18.1 kg.); the greatest, 69 pounds (31.3 kg.); and the least, 19 pounds (8.6 kg.). Twelve of the 15 patients had experienced normal menstrual function prior to the onset of the amenorrhea, and in three the menstrual function previously had been abnormal. Amenorrhea had been present from one to five years.

Examination of these patients revealed evidence of marked loss of weight, the appearance of age, pallor without anemia, dryness of the skin and hair, intolerance to cold, low blood pressure, and pulse rate. They were apathetic in appearance, and presented various gastrointestinal symptoms such as fullness after eating small amounts of food, anorexia, and fairly frequently vomiting and constipation. Examination of the pelvis revealed severe atrophy of the uterus, and the external genitals had an aged appearance.

Laboratory examination did not reveal anemia. The gastric concentration of acid was sometimes low, and the glucose tolerance curve was usually flat. The basal metabolic rate was low and tended to correlate with the duration

## AMENORRHEA NOT ASSOCIATED WITH PREGNANCY IN YOUNG WOMEN\*

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**A** MENORRHEA may be due to organic disease. Thus, it may be an early symptom in certain systemic conditions, disorders of metabolism, and tumors of the endocrine glands, or be related to pathologic changes. More commonly, an absence of the menses may be only an expression of physiologic disturbance of the glands primarily concerned with normal menstruation. Often it has been stated that menstrual function is not necessary for health. However, it should always be borne in mind, particularly if the patient is young, that amenorrhea may be a symptom of some condition that may adversely affect the health. Varying degrees of functional failure of the genital tract naturally may exist, and many patients come to the physician with menstrual irregularities. The duration and degree of such irregularities may vary within wide limits, and spontaneous remissions often occur. However, when amenorrhea has existed for a year or longer in young women, the fact should be evidence of a major derangement of function or of a disease process, and therefore merits a complete investigation.

The present paper is based on data for 94 young women between the ages of 19 and 25 years who came to the Mayo Clinic and who had not menstruated for a year or longer. They have been divided into five groups for the sake of a discussion of the conditions associated with their amenorrhea.

*Group 1. Primary Amenorrhea (19 patients).*—The young women of Group 1 had never experienced the menstrual function, though it is generally considered that the menses should be established spontaneously by the age of 19 years. This group of 19 patients offers a combination of developmental and functional defects that defies exact classification. Three of the 19 patients were found to have congenital absence of the vagina. Seven of the 19 patients presented normal secondary sex characteristics with no estrin or minimal amounts of this substance in the urine, together with marked hypoplasia of the uterus and atrophy of the endometrium. One of these seven patients had a large congenital cyst of the left tube and ovary that was removed. In six of the 19 patients, underdevelopment of the secondary sex characteristics was associated with hypoplasia of the uterus and endometrium and absence of estrin in the urine. The best that could be done to classify the remaining three of the 19 patients was to call them physiologic variants or tumor suspects. The values for 17-ketosteroids were elevated to more than 60 mg. in a twenty-four-hour specimen of their urine. One of them had the clinical characteristics of Cushing's syndrome, but the roentgenogram of the sella turcica and exploration of the adrenals and pelvic viscera gave entirely negative results.

Nine of the 19 patients previously had received hormone therapy for the amenorrhea without benefit. It is obvious that many combinations of develop-

\*Read (by invitation) at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

excessive stimulation. One may reasonably presume a fundamental fault in the ovary. The functional life of the human ovary is limited to approximately thirty-five years, but that it may be much less should be remembered.

*Group 5. Secondary Amenorrhea Associated With Failure of Gonadotropic Secretion by the Anterior Lobe of the Hypophysis (36 patients).—*Thirty-six patients experienced amenorrhea not associated with cyclic symptoms. This group we consider as having amenorrhea due to failure of the anterior lobe of the hypophysis to secrete gonadotropins. Thirteen of these patients (36 per cent) gave a history of abnormal menses prior to the onset of amenorrhea, compared to 70 per cent in the group primarily experiencing failure of function of the ovaries. Their general health had been considered to be normal, and the general physical examination did not reveal any abnormality. As a rule, the uterus was found to be considerably reduced in size. Roentgenograms of the sella turcica gave negative results in each case. In 20 of the 36 patients (56 per cent) the basal metabolic rate was markedly lowered, averaging -18 per cent, compared to only 29 per cent of the patients who primarily experienced failure of function of the ovaries. Twelve of these 20 gave a history of normal menses, and eight gave a history of abnormal menses prior to the onset of the amenorrhea. Gonadotropins and estrogens were either absent from the urine or present in minimal amounts. Microscopic examination of the endometrium revealed stages of poor proliferation, mixtures of proliferation and atrophy, or atrophy alone. The atrophy of the uterus and endometrium correlated with the low levels or absence of estrogens in the urine.

The lack of cyclic associated symptoms in these patients who had failure of gonadotropic function of the anterior lobe of the pituitary is owing to the lack of marked fluctuation in levels of estrogens and gonadotropins usually present in those patients previously described who experience ovarian failure. Perhaps in the 36 per cent of patients mentioned previously who experienced abnormal menses prior to the onset of amenorrhea, the anterior lobe of the hypophysis had always been at fault. It is not known whether the frequently associated lowered rate of metabolism is cause or effect.

It is difficult to explain adequately the failure of function of the anterior lobe of the pituitary in all of these patients. Some of them may be below normal in weight, but do not correspond to the anorexia nervosa group; others will be overweight, but obesity is frequently observed in women who have normal menstrual function. In the 56 per cent who were found to have lowered rates of metabolism this may serve to explain the situation, but it will not do so in the remaining 44 per cent.

### Comment

No doubt there are other combinations of disease and alterations of function than those mentioned here that will result in amenorrhea. In another series of comparable size the numbers of patients in each group might vary considerably. However, these patients serve to emphasize certain considerations.

The history often gives much useful information. If the menstrual history antecedent to the amenorrhea indicates normal function, it may be assumed that normal response of tissue existed at one time in the patient's life. If, on the other hand, the patient has never experienced normal function, it may be concluded that the tissues involved were not normal, were not subjected to normal stimulation, or did not live in an environment compatible with normal function. Unfortunately, the quality of tissue responsible for function of the genital tract with which women are endowed is not uniform. When cyclic premen-

and extent of the inanition. In this group of fifteen women it ranged from -12 to -40 per cent, with an average of -23 per cent. Microscopic examination of the endometrium revealed atrophy. Values for amounts of estrogens, gonadotropins and 17-ketosteroids in the urine were very low or, most frequently, these substances were absent. These findings indicate almost complete failure of function of the genital tract.

There is a tendency to consider the symptoms of these patients as due primarily to alteration in endocrine function, and the results of physical and laboratory examinations are adduced to prove the point. This is borne out by the fact that more than 50 per cent of this group of 15 patients had previously received endocrine treatment without benefit. The diagnosis of pituitary cachexia, Simmonds' disease, had often been made in these patients. Simmonds,<sup>1</sup> in his original description, showed that this condition was the result of a destructive lesion of the pituitary. Sheehan<sup>2</sup> expressed the belief that this lesion occurs most frequently as a result of shock and hemorrhage at the time of delivery. This author further commented that confusion appears to arise from the misconception that patients who have Simmonds' disease usually show cachexia. Fraser and Smith<sup>3</sup> suggested that the insulin tolerance test and estimation of the 17-ketosteroids may aid in differentiating between Simmonds' disease and anorexia nervosa.

Patients who have anorexia nervosa usually have a common starting point for their symptoms; namely, some difficulty of adjustment. They may have been overweight and initiated an ill-advised program of reduction that got out of hand, or they may have had some environmental conflict which led to a marked alteration in diet. The resulting starvation leads to varying degrees of alteration in all bodily functions, including that of the genital tract. The fact that all of these women had menstruated previously, 12 (80 per cent) having menstruated normally, would indicate that they had been endowed with essentially normal tissues.

*Group 4. Secondary Amenorrhea Associated With Failure of the Ovary to Function (17 patients).*—There were 17 young women in whom the amenorrhea was associated with cyclic symptoms such as nervous tension, menstrual molimina without flow, and vasomotor waves, a syndrome alluded to as the menopause when it affects older patients. The general physical examination revealed nothing characteristic. The examination of the pelvis usually revealed a uterus but little reduced in size. Seventy per cent of these patients who had ovarian failure gave a history of previous menstrual abnormality.

The basal metabolic rate was less than normal in five (29 per cent) of these 17 patients. Roentgenograms of the sella turcica gave negative results in each patient. Microscopic examination of the endometrium revealed varying stages of proliferation and occasionally subnormal secretory phases. Assays for amounts of estrogens in the urine gave varying results from none to normal or high normal amounts. High values for gonadotropins were found in 10 patients, and normal amounts were present in two patients.

The amenorrhea in these cases was considered to be primarily due to failure of the ovary to function. This, as is the case in women of the usual menopausal years, was often associated with the production of excessive amounts of gonadotropins. The values for amounts of estrogens and gonadotropins in the urine will fluctuate greatly, depending on the state of the ovarian-pituitary imbalance at the time the tests are made. These patients live in a more or less constant state of imbalance compared to the fairly even status of those patients who have amenorrhea due to failure of the pituitary to produce gonadotropins. It is this fluctuating imbalance that produces the symptoms associated with the amenorrhea in these women. There is failure of a glandular tissue living in an essentially normal environment and subjected to normal or

## Conclusions

When amenorrhea occurs in young women it should be considered as a major symptom. The patient merits a complete investigation, for amenorrhea may be associated with organic disease as well as with derangements of function.

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## Discussion

DR. JEAN PAUL PRATT, Detroit, Mich.—It is refreshing to listen to a discussion of amenorrhea without reference to treatment with endocrine preparations. Beginning with the purification and standardization of estrogens twenty odd years ago, a wave of symptomatic treatment was set in motion which is still rolling. Introduction of numerous natural, as well as synthetic, hormones has encouraged symptomatic treatment, so that it has, and still does, overshadow the importance of diagnosis and consideration of the patient as a whole.

One is impressed by finding 26 of the 94 patients classified as Groups 1 and 2. This raises two questions: Were the cases reported taken in series or selected, and what age limit was chosen?

Considering amenorrhea as a symptom, one looks for other symptoms or conditions to explain the amenorrhea. As Dr. Randall has shown, a complete examination of the patient is necessary. On the basis of the associated conditions, one might arbitrarily suggest three groups of amenorrhea.

Group 1 would include such structural defects as anomalies of the genital tract or tumors of the pituitary or adrenal, i.e., a real organic basis.

Group 2 might include primary amenorrhea associated with underdevelopment of primary and secondary sex characters. Many of these give a history of metabolic disturbances in earlier years. The damage was done during the developmental period. If recognized then, something might have been done to improve the development of the sex organs. If the period of growth and development has approached maturity, the possibility of developing the sex organs is small.

Group 3 could include all functional disturbances when development of the sex organs has been demonstrated by previous menstruation. This group would include most of Dr. Randall's Groups 3, 4, and 5. He has separated Groups 4 and 5 by relative amounts of gonadotropins and estrogens, as well as the relative size of the uterus and condition of the endometrium. Is the quantitative analysis of estrogens and gonadotropins and metabolic rate a sound basis for allocating the primary cause of amenorrhea to the ovary, pituitary, or thyroid? Can these glands function independently? Is the state of the uterus finally dependent upon ovarian secretion? It seems very difficult to distinguish these two groups.

Furthermore, in relation to the anorexia nervosa, the psychic factors are conspicuous and contribute to the patient getting into the state of malnutrition. Although psychosomatic factors are more difficult to measure quantitatively, their importance cannot be overlooked in any of the groups. It would seem desirable in all instances of amenorrhea, therefore, to look for the associated symptoms and conditions, to investigate the state of nutrition and environment and general health, to look for organic disturbances and treat them accordingly, to be observant of the finer shades of functional disturbance.

DR. FRANKLIN L. PAYNE, Philadelphia, Pa.—Review of the types of cases that are presented suggests that they were selected to emphasize certain points, rather than being taken chronologically. This is illustrated by the striking number of amenorrheas



strual symptoms without flow, nervous instability, and vasomotor waves are present, one suspects that the ovary is primarily at fault. If the patient has none of these symptoms it is more likely that the pituitary has failed to stimulate the ovary properly.

The physical examination alone often gives valuable information. In the experience of my colleagues and me, atrophy of the uterus occurs more rapidly in patients with failure of secretion of gonadotropin because of the accompanying absence of estrogens. This atrophy is much less marked in patients experiencing failure of the ovary. In these cases, larger amounts of estrogens are frequently found in the urine. This is further borne out by the difference in the types of endometrium in these two groups already mentioned.

The laboratory examinations help to indicate the amount of disturbance of function of the endocrine glands. In some instances they will reveal the reasons for amenorrhea, but often they still leave the physician without an actual explanation for its occurrence, except to state that certain glandular tissues have failed or inherently lack the capacity to function normally.

I have purposely avoided consideration that the thyroid gland is primarily at fault in those instances of low basal metabolic rate without myxedema. This may be in error. The results of proper elevation of the basal metabolic rate in the treatment of obstetric and gynecologic conditions are well known from the reports of Litzenberg and Carey,<sup>4</sup> Haines and Mussey,<sup>5</sup> and others. However, the thyroid is not primarily a gland related to the reproductive system. Patients whose basal metabolic rates are considerably lower than the accepted normal frequently are seen who clinically have no general or gynecologic and obstetric evidence of physiologic imbalance. The internists have stated certain criteria for the clinical diagnosis of low basal metabolic rate without myxedema, such as intolerance to cold, dry skin and hair, and fatigability. To those may be added evidence of abnormal function of the genital tract. However, when we come to consider cause or effect, that is to say, primary hypophyseal dysfunction or primary thyroid dysfunction, a residue of 44 per cent of patients with evidence of hypophyseal failure to secrete adequate amounts of gonadotropins in the presence of normal rates of metabolism, we are left somewhat in doubt.

Amenorrhea is often considered to be static and, because the patient does not menstruate, it is considered that the functional failure remains *in statu quo*. The physiologic conditions with which amenorrhea occurs may change in the same individual during an episode of amenorrhea. Some cases fulfill the criteria for a diagnosis of failure of the hypophysis to secrete normal amounts of gonadotropins, but, while the patient is still without menses, vasomotor waves may develop and excess amounts of gonadotropins will be found in the urine. Other cases of amenorrhea will fulfill the physical and laboratory requirements for a failure of the anterior lobe of the hypophysis, but in the history will appear an episode clinically suggestive of hyperfunction of the hypophysis as a result of failure of the function of the ovary.



onset of the pulmonary tuberculosis some of these patients would miss an occasional period, while others would have an amenorrhea of three months frequently, and still others six months or longer. As far as could be determined clinically, there was no pelvic disease to explain this behavior.

The two tables list the relationship of the onset of amenorrhea, of the patient's awareness to her illness in both age groups, of 14 to 19 years, and 20 to 25 years, and correlated to the prognosis. The first table gives the respective numbers in the various categories.

TABLE I. ONSET OF AMENORRHEA IN 62 WOMEN WITH PULMONARY TUBERCULOSIS. COMPARISON OF PROGNOSIS WITH 14-TO-19-YEAR AND 20-TO-25-YEAR AGE GROUPS

PROGNOSIS SYMPTOMS	FAVORABLE			UNFAVORABLE			DEAD			TOTAL		
	FIRST	EARLY	LATE	FIRST	EARLY	LATE	FIRST	EARLY	LATE	FIRST	EARLY	LATE
Ages 14 to 19												
17	3	3	3	1	2	1	1	1	2	5	6	6
Ages 20 to 25												
45	1	9	9	0	2	2	2	7	13	3	18	24
Totals												
62		28			8			26		8	24	30

TABLE II. PER CENT OF WOMEN IN AGE GROUPS 14 TO 19 AND 20 TO 25 HAVING SYMPTOMS OF AMENORRHEA IN RELATION TO PULMONARY TUBERCULOSIS

	SYMPTOMS			TOTAL
	FIRST	EARLY	LATE	
Ages 14 to 19	5	6	6	17-27%
Ages 20 to 25	3	18	24	45-72%
Totals	8	24	30	62
	13%	39%	48%	

The second table expresses percentages of the symptoms. It will be noted that 42 per cent of the women died. However, 13 per cent had amenorrhea as the first symptom. One-half of those who had amenorrhea early could have been benefited by earlier diagnosis. There is a slight suggestion that the younger group is more likely to develop amenorrhea early.

From these findings, amenorrhea in young women may be a symptom of a serious disease elsewhere in the body rather than one of the endocrinal or reproductive systems. Accordingly, the causes of amenorrhea in young women should be considered seriously and completely.

DR. RICHARD W. TELINDE, Baltimore, Md.—I would like to ask Dr. Randall whether he feels that cyclic therapy with estrogens and progesterone for Groups 4 and 5 has any value.

We have had great difficulty in distinguishing between those two groups. One of our cases with more than two years of amenorrhea and with marked shrinking of the uterus was placed on cyclic therapy. After several months of this she began to menstruate spontaneously and her uterus is again normal in size. We have recently curetted her and found that she has secretory endometrium, but she has failed to become pregnant.

DR. JOE V. MEIGS, Boston, Mass.—Dr. Albright of the Massachusetts General Hospital has done a lot of work on the FSH test and he believes there are three groups. The first group has the highest FSH amenorrhea due to ovarian failure, the second group has no FSH, the amenorrhea being due to failure of the pituitary gland. There is a third group who have a normal FSH, and he believes that there is a lack of luteinizing hormone. Ovulation does not take place, and ovulation is necessary to produce menstrual periods. He believes that this group is due to some failure of the hypothalamus.

that were associated with tumors (7 of 94 patients), two of which presented no other symptoms. It would be helpful to know the total number of amenorrheic patients from which these cases were collected. The occurrence of early tumors in the pituitary area that are silent—except for menstrual alterations—is interesting. The statistical frequency of such occurrences would add weight to their importance as diagnostic problems.

The large number of patients with anorexia nervosa (15 of the 94), suggests the selection of cases also. This group seems to present a picture of psychological maladjustment, at times associated with minor endocrinal malfunction, leading to marked dietary abuses that result in profound protein and vitamin deprivation, with ultimate female endocrinal failure. They seem to be more psychiatric or medical than gynecologic problems.

The remaining patients are divided into primary and secondary amenorrhea, with further division of the second group into those due either to ovarian, or to pituitary failure. This division is based upon symptomatology, pelvic findings, and endocrinologic studies. Analysis of the results of these studies reveals some of the many obstacles to a precise etiologic classification, and probably accounts for the broad term "failure," that Dr. Randall has chosen to use. These difficulties are most apparent in the ovarian group, with cyclic symptoms but no flow. The uteri were but little reduced in size, the endometrium showing varying stages of proliferation, and occasional subnormal secretory phases. The urine estrogen and gonadotropin assays ranged from normal to high normal, and basal rates were subnormal in 29 per cent of the patients. The uniform features are the symptoms and the uterine size, but the lack of uniformity of the other features suggests varying degrees of failure of the ovaries to perform normally, such as hypofunction, noncyclic function, or incomplete cyclic function. All of these alterations may be primarily ovarian, but one finds no proof that at least some of them do not result from pituitary or thyroid dysfunction.

In the group whose amenorrhea was attributed to anterior lobe failure, studies showed a general reduction in uterine size, with deficient endometrial changes and absent or minimal quantities of gonadotropins and estrogens. The uniformity of these results indicates ovarian hypofunction, possibly secondary to failure of the pituitary gland to perform normally. The associated subnormal basal rates in 56 per cent of the patients may be a reflection of pituitary failure, or the reverse may for some be the case, or the two may have a common etiologic background.

It is the general impression, based upon both clinical and experimental evidence, that the thyroid gland is essential to normal reproductive physiology. The role of thyroid dysfunction, whether this be primary or secondary, in functional amenorrhea has been demonstrated abundantly by its great frequency, and by the gratifying results of its treatment. In the present series both groups of the secondary amenorrheas numbered 53, and 47 per cent of these presented basal rates below minus 10 per cent. This figure is in line with the 44 per cent of subnormal basal rates in 66 patients with absent periods, as cited by Fluhmann five years ago. He was able to effect cures in 71 per cent of these, by means of thyroid therapy. No other therapeutic measure approaches these results in this condition. Steady progress is being made in the field of gynecologic endocrinology, and Dr. Randall's contribution is an important step in this progress. The cards are still stacked against us however, in the management of functional amenorrhea. It is well to play the thyroid cards to the full limit of their value, until further investigation enables us to deal better hands.

DR. HENRY C. HESSELTINE, Chicago, Ill.—Dr. Randall's title is all-inclusive. As he states, amenorrhea is a symptom and not a disease. Because his survey revealed only certain states which were associated with amenorrhea, I wish to add some of the observations made by Dr. Spear and myself upon young women with pulmonary tuberculosis.

This study was started while I was a member of Dr. Plass' department, at the University of Iowa, a number of years ago. We had a total of 134 women from 14 to 25 years of age, inclusive. Seven of these 134 patients had menorrhagia, while 65 had no menstrual cycle irregularity. The remaining 62 young women developed secondary amenorrhea. These 62 had regular menstrual cycles prior to their illness. It is evident now that after the

## CONSTRICTION RING DYSTOCIA\*

M. PIERCE RUCKER, M.D., RICHMOND, VA.

CONSTRICTION ring dystocia is that form of soft part dystocia characterized by the formation within the uterus of one or more bands of uterine muscle. These bands form opposite depressions of the fetal ovoid and may occur at any level. The band may entirely encircle the fetus or may extend only partially around the fetus, but in either case, so long as the ring lasts, the fetus is effectively anchored to the uterus, and there is no further progress in birth in spite of painful uterine contractions. A constriction ring (or contraction ring) is not a Bandl's ring, although the twentieth edition of *The American Illustrated Medical Dictionary* states that they are synonymous. Bandl's ring is an anatomic concept. It is located at the junction of the active contractile portion of the uterus with the lower uterine segment. As is well known, Bandl's ring ascends in obstructed labor, and the lower uterine segment becomes thinner and may eventually rupture. On the other hand, a constriction ring does not rise, but remains fixed to the fetus, and spontaneous rupture of the uterus does not occur. On account of the confusion in terminology, Rudolph suggested that the term constriction ring be revived. A constriction ring may be reversible or irreversible.

### History

This condition has been known since the beginning of modern obstetrics. The early writers called it irregular contraction of the uterus. Reynolds and Newell used the term constriction ring in their textbook in 1902. William Smellie tells of being called to one of the workhouses to see a woman who had been in labor five days. The midwife told him that the woman had lost a great deal of blood the night before. The head was low in the pelvis. He first tried to deliver with the forceps, but was surprised that he did not succeed, as the head was not large and the instrument was easily introduced. "Not succeeding in the above method, I opened the head, and, in trying to deliver it with the assistance of my fingers and the blunt hook on the inside of the skull, I could not, with all my strength, bring it along. However, by extracting the occipital and one of the parietal bones, I had room to introduce my hand, so as to find with my fingers the under part of the uterus strongly girt or contracted round the neck of the fetus. This I gradually dilated: then, bringing down one of the arms and pulling at that and the shattered bones of the scalp with both my hands, I at last extracted the child with greater ease than I expected."

"In pushing up my hand to dilate, my fingers passed the mouth of the womb that was girt round the middle of the head, when I was surprised to find another contraction before the shoulders. This was the first time, I observed, that different parts of the uterus would contract so strongly, a constriction which has been commonly ascribed to the mouth of the womb." This was in 1743. Even as late as 1908, Andrews and Maxwell reported using every instru-

\*Read at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.

DR. FREDERICK H. FALLS, Chicago, Ill.—There is another group of young women with amenorrhea not mentioned by Dr. Randall—the morphine addicts. These women have menstruated normally before they took up the morphine habit, and they became normal again after they could no longer get the drug. Therefore the amenorrhea cannot always be ascribed to an endocrinologic abnormality or to a malformation.

DR. RANDALL (Closing).—The group of patients presented here were selected on the basis of having been sufficiently investigated and followed up and, as indicated, we have to emphasize certain features of the problem of amenorrhea in the young woman. Naturally the groupings, as far as those cases with functional failure are concerned, are somewhat difficult to make.

Dr. TeLinde has raised the question of cyclic therapy. We use this a great deal in the treatment of these cases, but treatment was not mentioned in this paper for lack of time.

The question of the hypothalamus is important, of course. We talk about the pituitary being the master gland, but frequently must go beyond that to find the trouble such as, for example, the possible effect of morphine addiction, as mentioned by Dr. Falls.

Certainly one will agree with Dr. Payne that thyroid therapy is one of the best weapons we have for treating these patients. One wonders if we do not too frequently take the basal metabolic rate at its face value instead of realizing that it fluctuates greatly in many people, and that the significance of a given basal metabolic rate must be considered for the individual patient. There may be groups of women who require a lower or higher basal rate for normal function.

says the pains are characteristic in that the painful sensation continues after the palpable hardening of the uterus has passed off. While such pains are suggestive, they are not pathognomonic. I have seen such pains when there was no ring present. Torpin has shown that, when such pains are present, there is an intrauterine pressure of some 18 mm. of Hg., whereas normally between pains the intrauterine pressure is only 5 or 6 mm. of Hg. If, upon vaginal examination, the cervix hangs loosely about the presenting part, the suspicion that a constriction ring is present is heightened.

The ring was felt in 199 cases. Three other cases were so characteristic, even though the rings were not felt, that they are included, for they illustrate a practical point in management of such cases.

TABLE I

TOTAL CASES 13,575			
Induced labor	7,354 (54.2%)	Labors not induced	6,221 (45.8%)
By amniotomy 5,111 (37.7%)			
By Voorhees' bag 2,244 (16.5%)			
Constriction rings	102	Constriction rings	100 (1.61%)
After amniotomy	73 (1.46%)		
After bags	29 (1.25%)		
Pituitrin in first stage	Total 748	Constriction ring	21 (2.8%)
Dry labors	Total 483	Constriction ring	13 (2.7%)
(Spontaneous ruptured membranes)			

CASE 1.—No. 4738, a 31-year-old unmarried multipara, whose pelvis and blood pressure were normal, was seen Feb. 5, 1927, in labor. The waters had ruptured spontaneously forty-eight hours previously. After a 47¾-hour labor, the cervix seemed to be fully dilated upon rectal examination. She was given a perfect sacral anesthesia. The cervix was fitting loosely about the head, which was in left occipitoanterior position. Simpson's forceps were applied and the cervix was stripped back over the head easily. Extraction was difficult. Two loops of cord were found tightly drawn about the neck. One was cut between clamps, and the cord was unwound from about the neck. I was then greatly surprised to find that I was still unable to deliver the baby, nor could I rotate it. Kristeller maneuver was ineffectual and the combined bearing down by the patient and traction on the head failed to budge the body. Five minims of epinephrine (1:1000) were then administered, and in three minutes I was able to deliver the now dead baby without difficulty. The baby was a male and weighed 8 pounds, 14 ounces. The third stage and the puerperium were uneventful.

CASES 2 AND 3.—No. 5230 and No. 5216 were similar, except that labor was induced with a bag, and there was no cord about the neck to confuse the picture. Both resisted delivery by forceps until epinephrine was given, and then the operation was easy. One baby was stillborn and the other lived. The following case is more conclusive in that the ring was actually felt.

CASE 4.—No. 15967, a 29-year-old primipara, was admitted to the Johnston-Willis Hospital May 22, 1941, having pains every five minutes. Her pelvis was normal. Her blood Wassermann was negative. Her blood pressure and urine had been normal during her pregnancy, and before that for that matter, as she was treated for closed tubes for several months before she became pregnant. After eight hours, the cervix was fully dilated and the head was on the perineum. Forceps were applied and an episiotomy was done, but the head did not descend upon traction. The forceps were removed, and the interior of

ment they had except a punch in dealing with a ring that extended obliquely in a groove of the fetus between the thorax and the flexed thigh.

Sheldon reports the following case from the Boston Lying-In Hospital. "Mrs. G., aged 35 years, gravida v, para v, was admitted at term, in active labor. The presentation was transverse, with the head in the left iliac fossa. The pelvic measurements were normal. Twelve inches of umbilical cord prolapsed soon after admission. Vaginal examination revealed full dilatation of the cervix. Internal podalic version failed because of a contraction ring. The cord stopped pulsating. Several attempts were made at high forceps delivery, all failing because of the inclination of the symphysis. Version was again attempted. As this was unsuccessful, craniotomy was performed, but the cranio-elast continually slipped off the skull. Version was tried a third time. After several attempts to push the head through the contraction ring, 'a snap was heard and the head was felt in the peritoneal cavity.' A laparotomy was immediately performed, and a stillborn infant, weighing  $7\frac{1}{2}$  pounds, was extracted. A transverse tear was found in the lower uterine segment, dissecting behind the bladder and communicating with the bladder at one point. A supravaginal hysterectomy was performed, and the ruptured area in the bladder was sutured. Vaginal and abdominal wicks were inserted. The patient, postoperatively, drained urine both by vagina and through the abdominal incision. An indwelling catheter was placed in the bladder. She developed pneumonia, acute local peritonitis, and cystitis. She ran a febrile course for three weeks . . . but she finally recovered." This was in 1931.

It is evident that we are discussing a gruesome chapter of obstetrics. Perhaps for this reason it has not been discussed by this Society. The nearest approach to a discussion is Dickinson's paper (1910) in which he recommended cesarean section in a limited number of cases in which the infant is not definitely enfeebled or endangered by the length of labor, long drainage of amniotic fluid, or unskilled attempts at extraction. If the ring fails to relax under morphia or yield under complete etherization coupled with patient manual dilatation by a skilled obstetrician, a section is indicated, provided the mother be in fair condition for a laparotomy. He reported one such case. He concluded that there was a "clinical necessity of a clear formulation, or pronouncement concerning the import, diagnosis, and treatment of this condition, not only in the mind of the practicing obstetrician, but in that of the author of the textbook." The need that Dr. Dickinson voiced thirty-six years ago still exists.

I wish to discuss here 202 cases of constriction ring dystocia that I have seen in the past 43 years. These occurred in 13,575 term and near term deliveries.

### Frequency

This depends somewhat upon whether the condition is looked for or not. My first 20 cases, when the recognition of the ring was practically forced upon me, occurred in 2,737 deliveries; an incidence of 0.73 per cent. I was on the lookout for the next 182 cases. These represent 1.67 per cent of 10,838 cases (Table I).

### Diagnosis

The diagnosis is made with certainty upon feeling the ring with the hand in the uterus. The condition should be suspected when there is no obvious cause for the failure of labor to progress in spite of hard "pains." Phillips

of 15 per cent. Harper, who recommended delivery from below after the ring was relaxed with deep ether anesthesia, said that the fetal and maternal mortality in his cases was negligible. Herman Johnson recently reported 105 cases in private practice with no maternal mortality and a fetal mortality of only 5 per cent.

### Treatment

Constriction rings may occur at any time in the three stages of labor. When it is suspected early in the first stage, on account of the character of the pain and the lack of progress, the patient should be given morphine, demerol, or magnesium sulfate intravenously, and encouraged to sleep. Rudolph has shown that most constriction rings are reversible. If the patient is not allowed to become dehydrated, there is no reason to worry about the length of labor. After a good rest, labor is apt to progress in a more normal manner.

When the ring appears late in the first stage, or after the cervix is fully dilated, two lines of treatment are possible. One is to rest the patient and keep up the fluid intake and the electrolyte balance. Rudolph reports excellent results from this method. On the other hand, if the constriction ring can be relaxed, the baby can be delivered from below with greater safety than subjecting it to an 8- or 10-hour second stage while the ring is relaxing spontaneously. Dragging the baby through a ring that is not relaxed is not good obstetrics.

The ring can be made to relax in various ways. Beeson reports a case in which he relaxed the ring with chloroform and delivered the baby by version and extraction. There are several such cases in my series, but chloroform has failed in my hands oftener than it has helped. Harper was able to relax the rings in all his cases except one with deep ether anesthesia. My experience with ether has been similar to that with chloroform; it sometimes works, but more frequently it does not. It is interesting to note that in the 10 cases in which spinal anesthesia was used, it had no effect upon the ring. Souter reported excellent results with amyl nitrite. Barnes and Croft reported success in some cases and failures in others. Miles Phillips is of the opinion that it always works, provided enough be used. Sometimes as many as 5 ampules (5 minims) may be necessary. I have had no experience with this drug. Abarbanel's work would indicate that magnesium sulfate should be useful. I have tried it with success in suspected cases early in labor, but never as a preliminary to delivery. I believe it has merit and should be kept in mind.

Epinephrine (1:1000), administered subcutaneously in 5 to 8 minim doses, has been the most reliable relaxing agent in my experience. It was used in 150 cases. In seven, it was necessary to give a second injection, and in eight it failed to relax the ring. The action is prompt and should appear in from three to five minutes. Torpin tells me that he recently had a case in which the relaxing effect was delayed for fifteen minutes.

My cases fall into two groups; before and after the advent of epinephrine. In the first group we had no means of relaxing the ring other than anesthesia and manual dilatation. In this group there were 20 cases, with one maternal death and nine babies lost. In the second group there was no maternal death. The fetal death rate was 17.5 per cent. Eleven of the 32 infant deaths occurred in the first 23 cases.

The fatal case was that of a Negro woman, the mother of 13 children, who was admitted to St. Philip Hospital after failed forceps and version elsewhere. The ring did not relax under deep chloroform anesthesia and the fetus, which was macerated, was delivered by craniotomy. The mother did not recover from the anesthesia.

One of the cases in which epinephrine failed ended up with a Porro operation. This was a 37-year-old trained nurse, who had had an ovarian cyst

the uterus was explored. A constriction ring was found. Seven minims of epinephrine (1:1000) were administered hypodermically. The forceps were reapplied and an easy extraction was done. The puerperium was normal, and the mother and baby were discharged from the hospital in excellent condition on June 2.

### Etiology

Many causes have been advanced—the administration of ergot or pituitrin, rupture of the membranes, bag, and intrauterine manipulation, and malposition. These “causes,” with the exception of the administration of ergot, are represented in my cases. These are shown in Table I.

TABLE II. POSITION OF THE FETUS

TOTAL		203
Cephalic		181
ROA	18	
LOA	43	
ROP	56	
LOP	60	
Brow	1	
Face	3	
Breech		15
Transverse		3
Not stated		4

There were only 61 occipitoanterior positions in the 199 in which the position was recorded. Favorable position of the fetus occurred in only 30 per cent of the cases. There was a similar, but not so marked a deviation from normal in the pelves. The type of pelvis was recorded in 139 cases. Of these, 87 were normal, 28 were funnel, 18 justo-minor, four were flat, and two were flat rachitic. The average age of 201 patients was 28.43 years, which is a little over two years above the average for the whole series. The youngest was 17 years and the oldest 42 years of age. One hundred and thirty-four were primiparas. Something is known concerning the subsequent pregnancies of forty patients. This seems to be a small follow-up, but 13 were single and 60 were seen in consultation. The 40 patients had 47 subsequent pregnancies. The outcome of two of these pregnancies is not known. There were 8 abortions, 3 stillbirths, and 34 liveborn babies. In none of these subsequent labors was there dystocia, although one labor was prolonged. This would seem to indicate that the cause of constriction rings is a temporary one and not connected with the anatomy of the pelvis, or the uterus and its innervation. There is no common factor, not even long labor, that might be considered as a possible cause. The group on the whole presents a somewhat unfavorable selection as obstetric risks—increased age, abnormal presentations, and a larger number of borderline pelves—which fits into a working hypothesis that the ring is a fatigue phenomenon, comparable to the spasms that occur in striated muscles in runners or swimmers. Clinically, such a hypothesis is useful as a guide in the management of the case.

### Prognosis

The prognosis in cases of constriction ring dystocia depends upon a correct diagnosis and the institution of proper treatment. The earlier writers reported extremely bad results: White, an infant mortality of 72 per cent, a maternal mortality of 31.5 per cent; Michael, a fetal mortality of from 40 to 86 per cent and a maternal mortality of from 20 to 33 per cent. As late as 1941, McGill reported a fetal mortality of 46 per cent and a maternal mortality



## Summary

Two hundred two cases of constriction ring dystocia are analyzed in regard to frequency, diagnosis, and treatment. The frequency was found to be 1.67 per cent. There is a general impression that this condition is rarer than my figures would indicate. It is quite possible that many cases are overlooked. Cases are cited to show that some difficult forceps operations may be rendered easy if the constriction ring be relaxed with epinephrine. Epinephrine was used to relax the constriction ring in 150 cases. It failed eight times. Twenty cases occurred before it was known that epinephrine would relax the ring. Of these, one mother and nine babies were lost. One hundred eighty-two mothers and 183 babies (one set of twins) were seen after the advent of epinephrine. There was no maternal death, and the fetal mortality was 17.5 per cent. Eleven of these infant deaths occurred in the first 23 cases. As experience with this drug grew, the results improved.

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## Discussion

DR. SAMUEL A. COSGROVE, Jersey City, N. J.—Dr. Rucker deserves our thanks for clearly differentiating by definition three types of uterine rings which have been discussed under so many different terms, various authors having sometimes used different terms for the same entity.

His concept of the constriction ring which he describes as a fatigue phenomenon in the presence of such unfavorable factors as primigravidity, increased age, abnormal presentations, and borderline pelvises, would seem to be acceptable.

removed when she was in training. Two years after marriage and six years before I saw her, she was delivered of twins and had a postpartum hemorrhage. Her pelvis was normal and she was due by Naegele's rule the last of June, 1932. On March 4, she was admitted to the hospital on account of rupture of the membranes and was treated with bed rest, and was discharged undelivered on April 27. She began to have pains on May 9 and was readmitted. The cervix was two fingers dilated and a shoulder was presenting. A No. 5 Voorhees' bag was placed at 10:15 P.M. She was given  $\frac{1}{6}$  grain of morphine,  $\frac{1}{200}$  grain of hyoscine and avertin (60 mg. per kilo.). At 5:55 A.M. on May 10, the bag was removed without deflation. A knee was presenting. The patient was given ethylene, and both feet were brought down. They were shedding the skin. There was a tight ring about the thighs, which failed to relax when  $\frac{1}{2}$  c.c. of epinephrine (1:1,000) was administered hypodermically. The anesthesia was discontinued. A consultant suggested that pituitrin might be tried. Accordingly, 2 minims of pituitrin were given and extraction attempted. Both legs came off below the knees. A second consultant was called in, who performed a porro cesarean section. The female fetus had a meningocele, cleft palate, and iniencephalus. The mother made an uneventful recovery and was discharged from the hospital on May 29, 1932, in excellent condition.

TABLE III. METHOD OF DELIVERY

TOTAL	203
Version and extraction	131
Braxton Hicks' version	3
Breech extraction	11
Low forceps	14
Midforceps	39
Scanzoni	2
Craniotomy	2
Porro-cesarean section	1

TABLE IV. COMPLICATIONS

Retained placenta	9 (manual removal 7)
Placenta previa	3
Prolapsed cord	4
Postpartum hemorrhage	1
Eclampsia	3
Ablatio placentae	1
Toxemia	5
Hydramnios	3
Inversion of uterus	1
Phlebitis	1
Pyelitis	2
Mastitis	1
Febrile puerperium	16
Shock	1
Diabetes	3
Infantile paralysis	1

One other patient was delivered by craniotomy. She had a small pelvis and a dead baby, and had been in labor three days before admission to the hospital. The method of delivery of the 202 cases (one set of twins) is shown in Table III.

Complications accompanying these cases are shown in Table IV.

The nine cases of retained placenta with seven manual removals deserve some comment. All were due to hourglass contractions. There was no difficulty in manually removing the placenta, and no effort was made to relax the ring. Perhaps I should have given these patients another dose of epinephrine and attempted to deliver the placenta by Brandt's method, before resorting to manual removal.

and Pride have clarified a great deal of the confusion previously existing in retraction ring dystocia, but it has been to the essayist to point out further the more specific details in which retraction ring dystocia and constriction ring dystocia vary so greatly, although the frequency of either type exists in a small but very significant 1.67 per cent to 2 per cent of complicated dystocia cases. All of our cases of retraction have been relieved by rest under sedation, occasionally morphine or magnesium sulfate intramuscularly, or ether anesthesia with intravenous fluid, and when relaxation is established delivery is accomplished before the recurrence of the constriction or retraction ring. In no instance in our small series of dystocia due to this cause have we used epinephrine. There was definite increase in our stillbirth and neonatal mortality in retraction ring dystocia cases to 11.9 per cent.

Dr. Rucker gives a very timely warning not to drag the baby through an unrelaxed constriction or retraction ring but accurately to establish the diagnosis of retraction or constriction ring and to proceed with its relief with adrenalin injections. This has definitely lowered, in his hands the fetal mortality and consequently led to less maternal trauma and sequelae following delivery.

DR. RUDOLPH W. HOLMES, Charlottesville, Va.—Dr. Rucker has made the extremely important point that constriction rings may cause dystocia. He justly emphasizes the difference between such constrictions and retraction rings. They are definitely dissimilar anatomic entities. Clinically, they do offer certain comparable attributes as obstructions to spontaneous or operative delivery. Both have a common attribute in that they are primarily purely physiologic, but secondly, may become intensely pathologic.

The retraction ring may occur in one place only—namely, at the junction of the upper and lower uterine segments. It is an invariable concomitant of all labors, even when labor is precipitate. In the latter case it is merely a phenomenon of nature. Where dystocia persists, the rise of the ring and the attenuation of the lower segment may lead to pathologic rupture of the uterus.

While retraction rings are solely products of labor, this is not true of constriction rings, which may develop only in the upper segment before or during labor, and may occur only *after* the membranes have ruptured. This assertion that contraction rings are sequential to the escape of the liquor amnii is substantiated by a study of frozen sections of the bodies of pregnant or parturient women. Clarence Webster, Barry Hart, Freeland Barbour, and many others have contributed invaluable studies of such hardened and serially sectioned cadavers. In no instance have constriction rings been found in such anatomic investigations, irrespective of the length of labor, where the membranes have been intact. Where the waters have drained away, either in pregnancy or in labor, the uterus will retract upon the fetus. At first, the succulent, perhaps edematous, decidua will mold itself into every sulcus of the fetal contour. As the uterus retracts the muscularis will likewise fill every fetal depression. When the uterine muscle is in tetanic contraction, the multiple constrictions become of profound pathologic importance.

It has been twenty years since I retired, but when in practice I tried all the then putative measures for producing uterine relaxations, and found none that were of such signal value as chloral hydrate combined with sodium bromide. I doubt not that chloral still vies with all putative drugs which are alleged to relax the uterus.

DR. RUCKER (Closing).—If I have succeeded in putting across the difference between a constriction ring and a retraction ring I am perfectly satisfied.

I do want to say that it is not necessary to have ruptured membranes for a constriction ring to form. I have seen a number of cases with unruptured membranes with definite constriction rings. Also, I wish to say that the common habit of administering pituitrin when there is no progress in labor is exactly the wrong thing to do. If there is a constriction ring, a part of the uterus is already tetanically contracted and you are only adding one more insult.

The detailed histories cited do not seem convincing. Smellie's "mouth of the womb that was girt round the middle of the head" and "the under part of the uterus strongly girt or contracted round the neck of the fetus" would seem quite obviously to be an incompletely dilated cervix and a physiologic contraction ring. Dr. Rucker makes the distinction between the constriction ring which does not change its relation to the fetus and the constriction ring which may so change its relation. But it is only under conditions of extraordinary stress that it does so. Both rings tend to adjust themselves "opposite depressions in the fetal void," and we have all, I am sure, observed the physiologic contraction ring "girt or contracted about the neck of the fetus."

There is no disposition to deny the occasional occurrence of the entity defined by Dr. Rucker as "constriction ring," definitely and objectively diagnosed by so astute an observer, by direct intrauterine palpation.

We have not, however, demonstrated Dr. Rucker's constriction ring with anything like the average 1.5 per cent frequency shown by him. His suggestion that we have overlooked many because we were not *looking for them* may be perfectly just.

There is, however, this danger. Dr. Rucker states in an earlier paper, "When, however, there is a contracted pelvis or other obstruction to labor, it is sometimes difficult to say whether the dystocia is due to the ring or the dystocia." Inasmuch as it is frequently difficult to rule out disproportion, too great concentration on the *ring*, so apt to occur concomitantly with factors of mechanical dystocia, may lead to oversight or delay in instituting management necessitated by the other mechanical dystocia.

The generally conservative attitude in management of these cases advised by Dr. Rucker is admirable. He has again drawn attention to epinephrine, which in his own hands, and that of some other observers, has been of signal usefulness.

Yet he has actually found it necessary to use some form of operative interference in 94.5 per cent of his cases; 83.5 per cent were versions or midforceps, the first especially disadvantageous under the conditions of prolonged, exhausting pathologic labor.

He has made no use of cesarean section, except a Porro in one case, because in another communication he properly says, "... cesarean section after intrauterine examination and manipulation is dangerous." This is, of course, true only of transperitoneal section. Had extraperitoneal section been employed in some of his cases complicated by mechanical dystocia, his fetal mortality of 17.5 per cent might have been materially reduced without compromise of his splendid maternal mortality of one-half of 1 per cent.

DR. NORRIS W. VAUX, Philadelphia, Pa.—The author makes a very clear-cut and distinct difference between retraction ring dystocia as described by Bandl and this specific constriction ring dystocia. Bandl, in 1875, described and defined a ring at the junction of the upper active uterine body and the lower inactive or silent lower uterine segment. This clinical observation and picture which Dr. Rucker describes so completely does not carry with it a definite pathologic course and, no doubt, in many instances has been completely overlooked or has been mistaken for a beginning incomplete or partial Bandl's ring.

However, as the author has already pictured the constriction ring as appearing in any portion of the corpus uteri in contradistinction to the retraction Bandl ring and the later relief by the administration of adrenalin, our few cases might have been of true contraction character which occurred always in long labors, in vertex or breech position, and always in those patients whose membranes had been ruptured for a long period of time. This last feature of premature rupture of membranes occurring previous to the presence of constriction ring, Dr. Rucker does not clearly specify.

In our clinic (Philadelphia Lying-In) we feel that retraction ring does not occur unless the patient has been in active labor a long time, thirty-six hours or more, some abnormality of position of the fetus and occasionally moderately contracted pelvis with a questionable fetopelvic dystocia, and that the membranes have ruptured for some hours previously.

For many years the obstetric world has been more or less confused with regard to the etiology of the retraction ring and that abnormality which embraces the anatomic, physiologic, and pathologic point of view. Schroeder, Braune, Homes, White, Fitzgerald,

Our nearest neighbor in North Dakota is Minnesota. During the formative years of our maternal welfare program, we had the practical and sympathetic help of Doctor Jennings C. Litzenberg. He gave us courage and criticism in large measure. He came to help us. His leadership was spiritual as well as intellectual. To us his name became synonymous with good obstetrics. We can pay him no finer tribute.

As a country doctor, I would like to see an intensification of the teaching of the fundamentals. I have talked with many recent graduates in medicine. Many of them have admitted that their clinical training in obstetrics has been inadequate. If this condition has been brought about by war, it may correct itself in another medical generation; if, however, it is the result of too much theory and not enough practice in the impressionable undergraduate years, we need to revamp some of our teaching. I am old-fashioned enough to believe that the chief function of a medical school is to prepare students to practice medicine.

The second factor in good obstetrics is a sustained professional interest. In a rural state, environment becomes important in developing it. A lone doctor in a community must not be allowed to become a lonely doctor, or else both he and his patients will suffer. The doctor must have postgraduate opportunities made available to him in such a manner that he can keep abreast of current thoughts and trends in obstetric practice without too long absence from his practice.

Finally, as a third factor in promoting good obstetrics, I would emphasize the importance of integrating all of the agencies which have for their object the improvement of obstetric practice under the leadership of the medical profession.

In 1935, we formed the North Dakota Committee on Maternal and Child Welfare. It was appointed as a special committee of the North Dakota State Medical Association and, one year later, won recognition as a standing committee. It is predominantly a committee of general practitioners. It is the advisory committee to the North Dakota State Health Department in matters of maternal and child welfare. Thus, in this important field, the most cordial relationships have been established and maintained between the State Health Department and the State Medical Association.

In 1935, we had a maternal mortality rate in North Dakota of 55 per 10,000 live births. We called the committee to an immediate attack on this problem. We divided the "fatal triad" among our membership, and requested them to prepare practical papers on infection, toxemia, and hemorrhage for presentation before the district medical societies of our state. We then obtained invitations from the thirteen district societies to present these papers before them, and we were careful to assign our speakers to societies other than their own on the well-established principle that "a prophet is not without honor, save in his own country."

In 1936, we recommended to the State Health Officer that funds be made available to bring outstanding clinicians to the state to conduct obstetric and

## ENVIRONMENT IN OBSTETRICS\*

JOHN H. MOORE, M.D., GRAND FORKS, N. D.

THE difference between rural and urban obstetrics is one of environment. I have practiced "rural" obstetrics for twenty-six years. I conducted my last delivery in the home of a patient twenty-four years ago. A postpartum hemorrhage so nearly killed her that, while I was giving hypodermoclysis with a homemade normal saline solution from a 20 c.c. syringe, I vowed that if the Good Lord would let me get out of that home with a living mother I would never go back to such primitive practice. He did, and I kept my vow.

Then I started to change the environment. I am still trying to change it. I have seen the small general hospitals of my city and my state develop from the point where they had no maternity departments, no birth rooms, no nurseries, to the place where many of them have well-equipped maternity departments, modern delivery rooms, excellent nursing supervision, and good staff organizations; in brief, a proper conception of the dignity and importance of obstetrics.

This has brought me to the conclusion that, aside from the factor of environment, there is no difference between rural and urban obstetrics. But there is a tremendous difference between good and bad obstetrics! I have seen both kinds in North Dakota and both kinds in the maternity departments of our best teaching centers. I believe that we, in North Dakota, have one advantage over our professional brethren in large cities: our mistakes quickly become public property. This makes for self-analysis and, we hope, for self-improvement.

It seems to me that good obstetrics is a composite of several factors. First, there is a sound knowledge of the fundamentals. This should be obtained in our medical schools. It implies that, in addition to sound classroom instruction, the student shall have the opportunity to observe obstetrics and to take part in the conduct of pregnancy, labor, and the puerperium under the direction of competent and enthusiastic instructors. In my section of the country, this type of instruction reached its highest efficiency in the Departments of Obstetrics and Gynecology at the Universities of Minnesota, Iowa, and Wisconsin. These institutions have become recognized factors in improving obstetric practice in their neighboring states of the Midwest. They have never lost the clinical approach to the problems of the general practitioner, nor personal interest in the undergraduate student. The leadership which they have given us came, rightly, from the heads of the Departments of Obstetrics and Gynecology. They imbued their staffs with an interest and enthusiasm for teaching clinical obstetrics that has paid dividends in a decreasing maternal mortality.

\*Read (by invitation) at the Sixty-Ninth Annual Meeting of the American Gynecological Society, Hershey, Pa., June 3 to 5, 1946.